

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2020

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE
TRANSITION PERIOD FROM TO

Commission File Number 001-39460

KYMERA THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)
200 Arsenal Yards Blvd., Suite 230
Watertown, Massachusetts
(Address of principal executive offices)

81-2992166
(I.R.S. Employer
Identification No.)

02472
(Zip Code)

Registrant's telephone number, including area code: (857) 285-5300

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	KYMR	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

The registrant's common stock was not publicly traded as of the last business day of the registrant's most recently completed second fiscal quarter.

The number of shares of Registrant's Common Stock outstanding as of February 26, 2021 was 44,811,485.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for its 2021 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2020, are incorporated by reference into Part III of this Annual Report on Form 10-K

Table of Contents

	<u>Page</u>
PART I	
Item 1. Business	3
Item 1A. Risk Factors	54
Item 1B. Unresolved Staff Comments	99
Item 2. Properties	99
Item 3. Legal Proceedings	99
Item 4. Mine Safety Disclosures	99
PART II	
Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	100
Item 6. Selected Financial Data	100
Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations	101
Item 7A. Quantitative and Qualitative Disclosures About Market Risk	112
Item 8. Financial Statements and Supplementary Data	112
Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	113
Item 9A. Controls and Procedures	113
Item 9B. Other Information	113
PART III	
Item 10. Directors, Executive Officers and Corporate Governance	114
Item 11. Executive Compensation	114
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	114
Item 13. Certain Relationships and Related Transactions, and Director Independence	114
Item 14. Principal Accounting Fees and Services	114
PART IV	
Item 15. Exhibits, Financial Statement Schedules	115
Item 16. Form 10-K Summary	116

SUMMARY OF THE MATERIAL AND OTHER RISKS ASSOCIATED WITH OUR BUSINESS

- We are a biopharmaceutical company with a limited operating history and have not generated any revenue to date from drug sales, and may never become profitable.
- We have incurred significant operating losses in recent periods and anticipate that we will incur continued losses for the foreseeable future.
- We will need to raise substantial additional funding. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, scale back or discontinue some of our product candidate development programs or future commercialization efforts.
- We are very early in our development efforts and our IRAK4, IRAKIMiD, and STAT3 programs are still in preclinical or early clinical development. If we are unable to advance them into and through the clinic for safety or efficacy reasons or commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- Our approach to the discovery and development of product candidates based on our Pegasus platform is novel and unproven, which makes it difficult to predict the time, cost of development, and likelihood of successfully developing any products.
- Business interruptions resulting from the coronavirus disease (COVID-19) outbreak or similar public health crises could cause a disruption of the development of our product candidates and adversely impact our business.
- We may not be successful in our efforts to identify or discover additional product candidates or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.
- If we experience delays or difficulties in the initiation or enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- Our current or future product candidates may cause adverse or other undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.
- Even if we receive regulatory approval for any of our current or future product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense.
- We rely, and expect to continue to rely, on third parties to conduct our ongoing and planned clinical trials for our current and future product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialize our current and potential future product candidates and our business could be substantially harmed.
- If we are unable to obtain and maintain patent and other intellectual property protection for our technology and product candidates or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “believes”, “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. These statements are not guarantees of future results or performance and involve substantial risks and uncertainties. Forward-looking statements in this Annual Report include, but are not limited to, express or implied statements about:

- the initiation, timing, progress, results, and cost of our research and development programs, and our current and future preclinical and future clinical studies, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- our ability to continue to construct Pegasus, our drug discovery platform, and to enable a rational and effective drug discovery and development engine;
- the timing and the success of preclinical and clinical studies under our IRAK4, IRAKIMiD, and STAT3 programs;
- our plans to submit investigational new drug applications to the FDA for current and future product candidates;
- the subsequent initiation of planned clinical trials;
- our ability to identify research priorities and apply a risk-mitigated strategy to efficiently discover and develop product candidates, including by applying learnings from one program to other programs and from one modality to our other modalities;
- our potential ability to manufacture our drug substances, delivery vehicles, and product candidates for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;
- the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to commercialize our products, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business, product candidates, and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- estimates of our future expenses, revenues, capital requirements, and our needs for additional financing;
- the potential benefits of strategic collaboration agreements, our ability to enter into strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- future agreements with third parties in connection with the commercialization of product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;

- our ability to produce our products or product candidates with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials;
- our expectations regarding the time during which we will continue to be an emerging growth company or smaller reporting company as defined in federal securities regulations; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

Any forward-looking statements in this Annual Report reflect our current views with respect to future events and with respect to our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part II, Item 1A, “Risk Factors” and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

All of our forward-looking statements are as of the date of this Annual Report only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Annual Report or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission, or the SEC, could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Annual Report, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Annual Report that modify or impact any of the forward-looking statements contained in this Annual Report will be deemed to modify or supersede such statements in this Annual Report.

We may from time to time provide estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this Annual Report. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

Item 1. Business.

We are a biopharmaceutical company focused on discovering and developing novel small molecule therapeutics that selectively degrade disease-causing proteins by harnessing the body's own natural protein degradation system. Our proprietary targeted protein degradation platform, which we refer to as Pegasus™, allows us to discover highly selective small molecule protein degraders with activity against disease-causing proteins throughout the body. We believe that our small molecule protein degraders have unique advantages over existing therapies and allow us to address a large portion of the human genome that was previously intractable with traditional modalities. We focus on biological pathways that have been clinically validated but where key biological nodes/proteins have not been drugged or inadequately drugged. To date, we have utilized our Pegasus™ platform to design novel protein degraders focused in the areas of immunology-inflammation and oncology, and continue to apply our platform's capabilities to additional therapeutic areas. Our initial programs are IRAK4, IRAKIMiD, and STAT3, which each address high impact targets within the interleukin-1 receptor/toll-like receptor, or IL-1R/TLR, and janus kinase/signal transducers and activators of transcription, or JAK/STAT, providing the opportunity to treat a broad range of immune-inflammatory diseases, hematologic malignancies, and solid tumors. Our programs exemplify our focus on addressing high impact targets that have been elusive to conventional modalities and that drive the pathogenesis of multiple serious diseases with significant unmet medical needs. With respect to our IRAK4 program, we are collaborating with Genzyme Corporation, a subsidiary of Sanofi S.A, or Sanofi, on the development of drug candidates targeting IRAK4 outside the oncology and immuno-oncology fields. We submitted an Investigational New Drug Application, or IND, to the U.S. Food and Drug Administration, or FDA, for KT-474 in 2020, and initiated the single ascending dose, or SAD, portion of our Phase 1 trial in adult healthy volunteers in February 2021. We also expect to submit INDs for degraders from our IRAKIMiD and STAT3 programs in the second half of 2021, and if cleared, to initiate Phase 1 trials in patients thereafter.

Our Strategy

Our mission is to discover, develop and commercialize novel and transformative therapies that improve the lives of patients with serious diseases, and we are committed to the selection of targets that enable a broad impact across multiple clinical indications with high unmet medical need. We believe the unique discovery capabilities of our Pegasus™ platform will position us to be a leader in the area of targeted protein degradation. Our goal is to become a fully integrated biopharmaceutical company with a pipeline of novel degrader medicines targeting disease-causing proteins that were previously intractable. We intend to achieve this goal by pursuing the strategic objectives set forth below.

- **Advance the development of our IRAK4, IRAKIMiD, and STAT3 programs to deliver transformative therapies to patients.** We maintain a core set of drug development principles which guide our protein target selection and our discovery and development efforts. We are specifically focused on delivering therapeutic solutions that reach previously inaccessible targets, in particular those in which the biological pathways are clinically and genetically well-validated, in order to address significant unmet medical needs within broad patient populations. We believe our IRAK4, IRAKIMiD, and STAT3 programs have the potential to treat multiple immune-inflammatory and oncology disease indications that fit these criteria. In February 2021, we initiated the SAD portion of our Phase 1 clinical trial for KT-474, our lead drug candidate in our IRAK4 program, in adult healthy volunteers. This is the first time that a heterobifunctional small molecule degrader has been administered to healthy volunteers. In the second half of 2021, we expect to initiate enrollment in the Multiple Ascending Dose (MAD) portion of the Phase 1 trial of KT-474, including healthy volunteers and a subsequent cohort of hidradenitis suppurativa, or HS, and atopic dermatitis, or AD, patients, pending FDA's removal of the partial clinical hold for this portion of the trial. We also expect to initiate Phase 1 clinical trials for degrader drug candidates from our IRAKIMiD and STAT3 programs, including KT-413, our IRAKIMiD development candidate following a planned IND filing in the second half of 2021, and in KT-333, our STAT3 development candidate following a planned IND filing in the fourth quarter of 2021.
- **Further expand the capabilities of our Pegasus™ platform to identify the optimal pairing of therapeutic targets with E3 ligases for a range of disease states.** Our targeted protein degradation, or TPD, platform, Pegasus™, enables us to identify an expanded library of E3 ubiquitin ligases, or E3 ligases, to discover highly selective degraders with activity against disease causing proteins throughout the body. Pegasus has the potential to help us better understand not only the optimal pairing of disease-causing protein targets with E3 ligases, but also the degradation profiles across different cell types and tissues, further enabling us to convert our differentiated E3 binders into novel degraders. We believe our ability to identify and utilize previously unliganded E3 ligases, particularly those with selective or restricted expression, may unlock new opportunities across broad therapeutic applications.

- **Continue to build a broad and diverse pipeline of novel protein degraders.** Guided by our drug development principles and the learnings from our IRAK4, IRAK1MiD, and STAT3 programs, we intend to continue to identify therapeutic targets that have disruptive therapeutic potential and are predicted to be well-suited for a TPD approach. Given the unique genetic profiles in some of the patient populations that we aim to serve, we plan to continue to leverage a precision medicine approach to help identify patients with the highest probability of responding to our degrader drug candidates. The capabilities of our discovery platform, such as our expanded toolbox that includes E3 ligases beyond the two predominantly used in the field today, cereblon and von Hippel-Lindau, or VHL, enable us to pursue targets linked to a wider range of indications.
- **Expand and protect our proprietary know-how and intellectual property.** We have developed a broad patent estate protecting our intellectual property, which we intend to expand to further protect our Pegasus™ platform and the drug candidates we develop. Our intellectual property, which includes proprietary know-how as well as a series of patents, applies to not only our invented compounds but also to our E3 Ligase Whole-Body Atlas and our E3 Ligase Binders Toolbox.
- **Pursue synergistic collaboration opportunities.** To further our goal of delivering transformative therapies to the broadest possible patient population, we intend to become a fully integrated biopharmaceutical company. As part of this plan, in addition to our ongoing collaborations with Vertex and Sanofi, we expect to leverage additional strategic partnerships that can contribute complementary capabilities in discovery, development and commercialization in disease areas both within and outside of our core areas of therapeutic focus.

Background of Targeted Protein Degradation

Proteins are responsible for the structure, function and regulation of tissues and organs. Cells in the body continuously synthesize and degrade proteins, maintaining an equilibrium called protein homeostasis. Most diseases are the result of aberrant protein behavior driven by activation, mutation, or downregulation of the protein itself, or by the gene responsible for the transcription and translation of that particular protein. With a deepened molecular understanding of various diseases and the characterization of the full human genome, research efforts have increasingly focused on the development of medicines to address malfunctioning proteins responsible for oncologic, auto-immune, cardio-metabolic, neurodegenerative, and rare genetic diseases.

The ‘druggable’ genome challenge

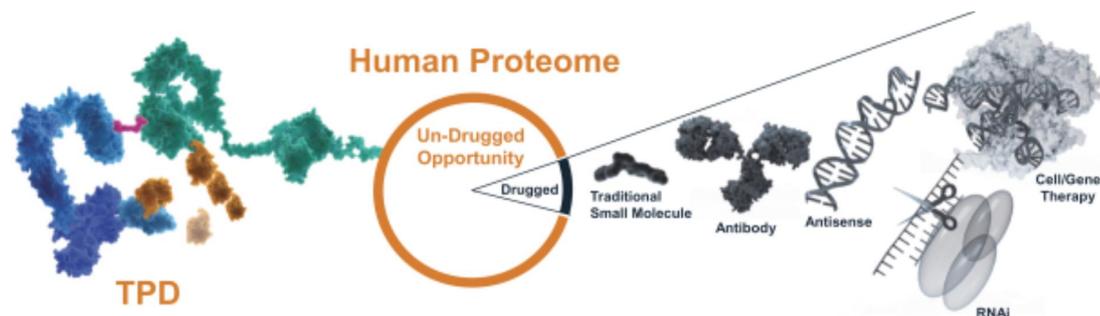
Several therapeutic modalities have been developed over the years to address aberrant protein activity. These have included small molecule inhibitors of protein function, therapeutic antibodies, oligo-based therapeutics such as RNA interference therapeutics, antisense oligonucleotides, or ASO, and other genetic therapies.

Some of these modalities have had a tremendous impact on the treatment of diseases and quality of life of patients, and several others, while earlier stage, offer potential. However, these traditional modalities face specific challenges that limit their therapeutic impact and reach. Some of the limitations of existing modalities include the following:

- **Traditional small molecule therapeutics** are unable to block the function of proteins without a catalytic or substrate binding site and cannot block proteins with dual function, as such are not effective against transcription factors, scaffolding and adaptor proteins, many of which play a key role in certain diseases.
- **Therapeutic antibodies** are generally too large to penetrate cells and are therefore typically limited to protein targets that are extracellular, or outside of the cell, whereas most proteins are inside the cell. They also have to be dosed parenterally and can be costly and complex to develop and manufacture.
- **Oligo-based therapeutics** are capable of drugging proteins elusive to small molecules in some cases but have significant drug delivery challenges with dosing and in achieving systemic distribution, greatly limiting the breadth of diseases they are able to address effectively. These therapeutics can also be costly and complex to develop and manufacture.

As a result of these limitations, we believe that only 20% of the full human genome has been effectively drugged to date. New therapeutic modalities which can overcome some of these challenges are necessary to expand the drugged proteome/genome and provide new efficacious medicines to patients in need. We believe that targeted protein degradation is such a modality.

Figure 1. Expanding the Druggable Human Proteome.



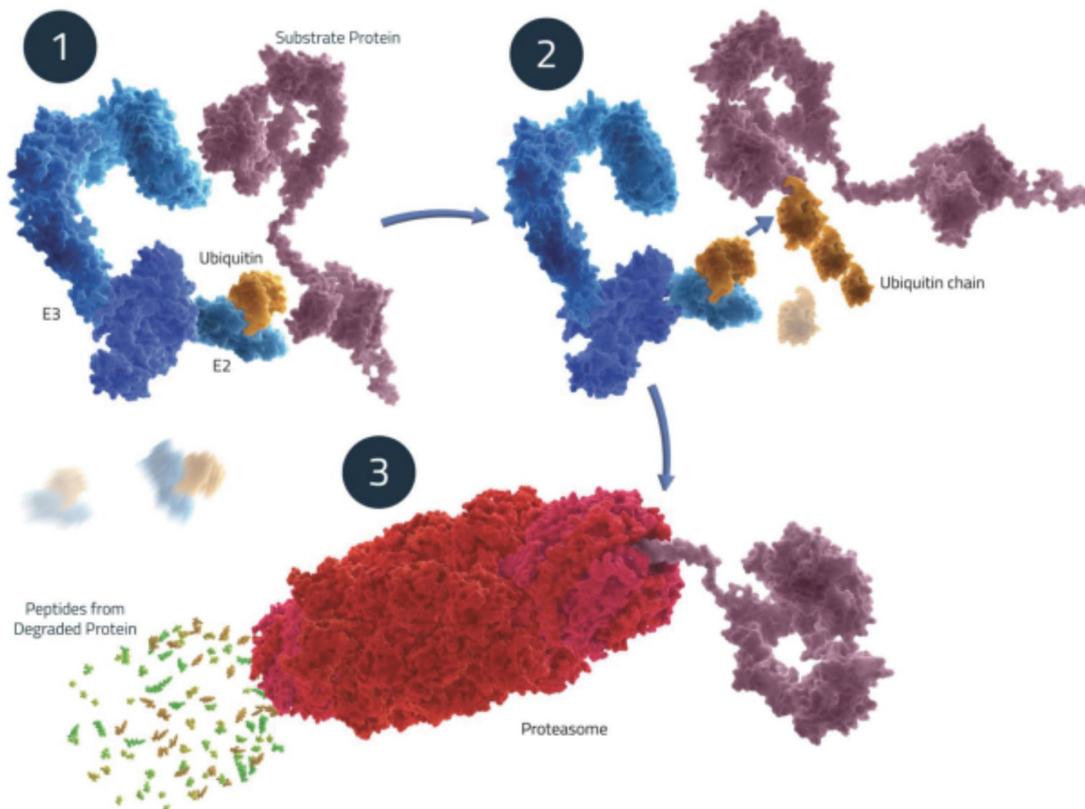
Targeted Protein Degradation

One of the methods that cells use to control the balance between the synthesis of new proteins and the degradation and disposal of damaged and/or misfolded proteins, is ubiquitin-proteasome system, or UPS. The discovery of ubiquitin-mediated protein degradation provided important insights into specific processes like cellular division and DNA repair and led to the discovery of UPS' critical roles in various cellular pathways, including the cell cycle, signaling pathways, the regulation of gene expression, and responses to oxidative stress. The discovery of the UPS also revealed a new modality to harness this cellular process for the treatment of diseases.

The UPS comprises a series of finely orchestrated enzymatic sequences that ultimately lead to protein polyubiquitination and degradation by the proteasome in cells. Protein ubiquitination is a cellular process involving an enzymatic cascade consisting of ubiquitin-activating enzymes (E1), ubiquitin-conjugating enzymes (E2), and ubiquitin-protein ligases (E3). In humans, there are two classes of ubiquitin activating E1 enzymes, more than 30 E2 enzymes, and approximately 600 E3 ligases.

As illustrated in the figure below, the E3/E2/ubiquitin ligase complex (shown in blue) binds to a substrate protein (shown in purple) to mediate the transfer of ubiquitin, which leads to degradation of the target protein through the proteasome.

Figure 2. Natural Protein Degradation Through Ubiquitin-Proteasome System.

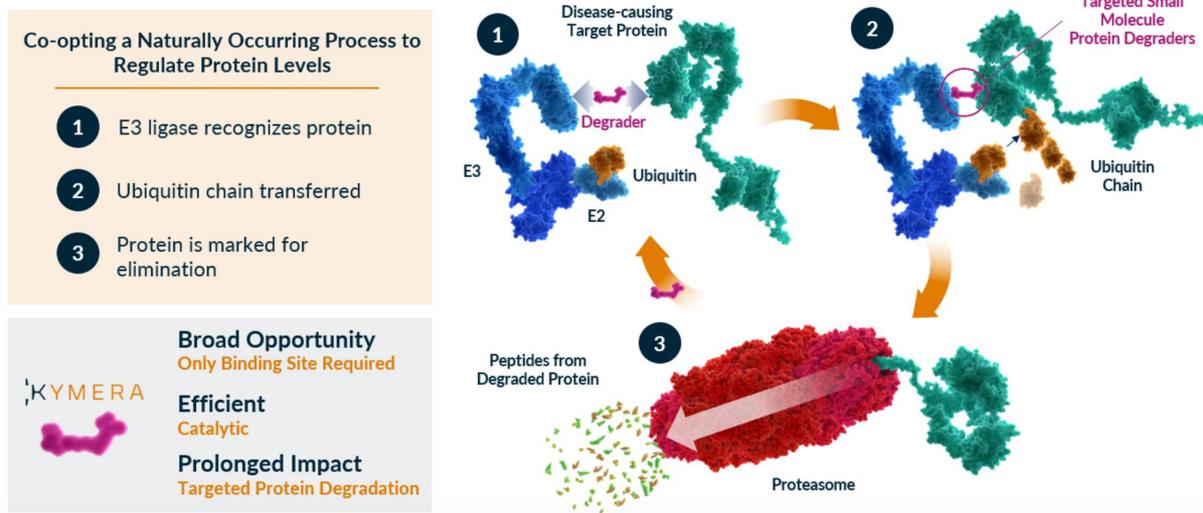


Targeted protein degradation is a new modality that co-opts this innate cellular process. The core of the TPD modality consists of a small molecule (shown in magenta in the figure below) that we refer to as a heterobifunctional degrader. The role of this heterobifunctional degrader molecule is to mediate a “new” interaction through the formation of a ternary complex between a disease-causing protein and an E3 ligase. The E3 ligase tags the protein target for degradation by attaching a series of ubiquitin, and the proteasome recognizes the tagged protein and degrades it into small peptides.

Forming an efficient ternary complex, as shown in step 2 in the figure below, is a critical step in TPD, and its formation, function, and effect on cellular and *in vivo* systems is vital to the success of the degradation and its impact on disease. In addition, the degrader molecule needs to be able to effect degradation in a variety of different cell types and contexts and have the right pharmaceutical properties to be therapeutically dosed to patients.

As shown in the figure below, after the degrader facilitates the ubiquitination of the target protein, and as the protein is degraded by the proteasome, the molecule separates from the protein, and is able to form another ternary complex to conduct the degradation process again. This iterative mechanism is catalytic, which results in increased potency even at lower concentrations, another key differentiator from other modalities such as small molecule inhibitors and therapeutic antibodies.

Figure 3. Overview of Targeted Protein Degradation.



Due to the unique advantages of targeted protein degradation, this transformative modality is capable of targeting proteins traditionally undrugged by small molecules. Specifically, TPD can target proteins without a catalytic function such as scaffolding proteins and transcription factors, with small molecule-like drug properties that can potentially be dosed orally and distributed systemically unlike oligo-based therapeutics such as RNAi's. TPD molecules also are amenable to existing small molecule manufacturing principles which are less costly than other therapeutic modalities. Because of the catalytic nature of the degradation process, we believe the modality has the potential to be therapeutically effective with smaller amounts of drug substance and less frequent dosing than traditional therapeutics.

The use of small molecules to affect protein homeostasis has been clinically and commercially validated by multiple drugs over the past two decades. Drugs such as bortezomib and fulvestrant have been understood to inhibit the proteasome and target the estrogen receptor for proteasome-dependent degradation, respectively. More recently, immunomodulatory imide drugs such as lenalidomide and pomalidomide have been understood on a post-hoc basis to direct the degradation of a series of transcription factors via the UPS.

These immunomodulatory drugs have validated the concept of using the UPS to degrade proteins and elicit a pharmacological and therapeutic effect in disease settings. However, unlike earlier approaches in this field, TPD takes this proven concept further to prospectively target the degradation of a wider range of proteins through the rational design of heterobifunctional degraders which coordinate the discreet binding of target proteins and E3 ligases to drive the desired protein degradation.

Currently, the field of TPD has largely been focused on the generation of heterobifunctional small molecule degraders against various targets by using the generally well-characterized E3 ligases, cereblon and VHL. Heterobifunctional degraders targeting either the androgen receptor or estrogen receptor for the treatment of castration-resistant prostate cancer or advanced breast cancer are currently in Phase 2 and Phase 1 clinical testing, respectively. Both degrader compounds are oral drugs administered daily with early signs of acceptable pharmacokinetics and safety and, in the case of the androgen receptor degrader, preliminary evidence of tumor growth inhibition.

An important factor for the efficiency of a degrader is the specificity and affinity to the targeted E3 ligase. The various E3 ligases have different distribution and cellular localization profiles that are important factors when considering which E3 ligase to use for a particular disease protein target. There are approximately 600 E3 ligases that occur in nature, but to date only a handful of these E3 ligases have been evaluated for therapeutic purposes, leaving a substantial portion of the genome available for targeting.

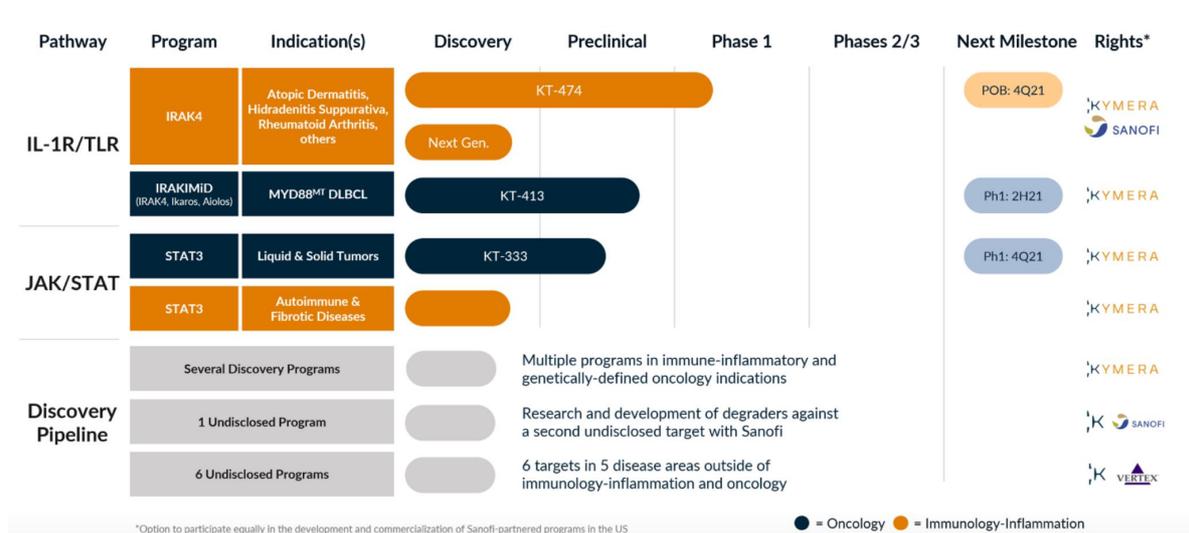
Our Pegasus™ Platform

Our proprietary Pegasus™ platform enables us to design highly active and selective molecules that utilize the UPS, the body's natural E3 ligase-directed protein disposal system, to target and degrade disease-causing proteins. E3 ligases bind to a target to mediate the transfer of ubiquitin, which leads to degradation of the protein through the proteasome. We believe our platform enables us to discover and develop novel protein degraders that optimize the use of the three essential elements of our small molecule protein degraders: an E3 ligase, a binding moiety, a target protein binding moiety, and a linker connecting the two. The key components of our Pegasus™ platform described below combine our broad understanding of the localization and expression levels of the hundreds of E3 ligases in the human body with our proprietary E3 Ligase Binders Toolbox, as well as our chemistry, biology, and computational capabilities to develop protein degraders that address significant, unmet medical needs.

- **E3 Ligase Whole-Body Atlas:** We have identified the expression profiles of approximately 600 naturally-occurring unique E3 ligases across different tissues. This knowledge enables us to match a target protein with the appropriate E3 ligase based on expression, distribution, intracellular localization, and biology.
- **E3 Ligase Binders Toolbox:** Our E3 Ligase Whole-Body Atlas has allowed us to generate a toolbox of proprietary ligands designed to bind to an expanded library of E3 ligases that we believe will enable us to develop novel small molecule protein degraders with specific degradation profiles.
- **Ternary Complex Modeling:** Our structural biology information, combined with biochemical, biophysical, and computational characterization of ternary complexes is used to prospectively design highly efficient and selective degraders.
- **Quantitative Systems Pharmacology Model:** Our understanding of the *in vitro* and *in vivo* pharmacokinetic/pharmacodynamic, or PK/PD, relationships of our degraders across different tissues and cell types has allowed us to build an understanding of the diverse parameters that impact protein levels, and to model these parameters in different species, including humans.
- **Proprietary Chemistry:** Our expertise in proprietary chemistry provides us the opportunity to design degraders with optimized pharmaceutical properties tailored to not only specific diseases but also potentially targeted patient populations.

Our Therapeutic Pipeline

Our initial programs are IRAK4, IRAKIMiD, and STAT3, which each focus on a single critical signaling node within the genetically and clinically validated IL-1R/TLR and JAK/STAT pathways. Our programs exemplify our focus on addressing high impact targets that have been elusive to conventional modalities and that drive the pathogenesis of multiple serious diseases with significant unmet medical needs. We believe degrading these targets has the potential to treat multiple immune-inflammatory diseases, hematologic malignancies, and solid tumors. In February 2021, we initiated the healthy volunteer Single Ascending Dose (SAD) portion of our Phase 1 clinical trial for KT-474, the lead drug candidate in our IRAK4 program. In the second half of 2021, we expect to initiate enrollment in the Multiple Ascending Dose (MAD) portion of the Phase 1 trial of KT-474, including healthy volunteers and a subsequent cohort of HS and AD patients, pending FDA’s removal of the partial clinical hold for this portion of the trial. We also expect to submit INDs for degraders from our IRAKIMiD and STAT3 programs in the second half of 2021, and if cleared, to initiate Phase 1 trials in adult cancer patients thereafter. We also have multiple programs in earlier stages of development and are exploring targets in therapeutic areas outside of our core areas of focus. The following table summarizes our development pipeline:



Our IRAK4, IRAKIMiD, and STAT3 Programs

We are developing KT-474, a highly active and selective, orally bioavailable IRAK4 degrader, for the treatment of IL-1R/TLR-driven immunology-inflammation conditions and diseases with high unmet medical need, including HS, an inflammatory skin disease, as well as AD and rheumatoid arthritis. We have chosen to pursue IRAK4 degradation due to the well-validated role of the IL-1R/TLR pathway in immunology and inflammation and the potential advantage that drugging a single node of multiple different mediators of inflammation has over other approaches focused on targeting one of many cytokines that stimulate the IRAK4 node. IRAK4 is a critical node in the IL-1R/TLR signaling pathway, which is dependent on both IRAK4’s kinase activity and scaffolding function. We have demonstrated through our *in vitro* and *in vivo* studies that KT-474 induces IRAK4 degradation, impacting both the kinase and the scaffolding functions, and therefore can efficiently and selectively block IL-1R/TLR-mediated inflammation in a way we believe to be superior to IRAK4 kinase inhibitors. We therefore believe KT-474 has the potential to improve outcomes over current treatment options as well as other drugs currently in development. We submitted an IND for KT 474 to FDA in 2020 and initiated the SAD portion of our Phase 1 trial in adult healthy volunteers in February 2021. We are collaborating with Sanofi on the development of drug candidates targeting IRAK4 outside the oncology and immunology fields. See “Business—Collaborations—Collaboration Agreement with Genzyme Corporation.”

We are developing another group of IRAK4 degraders, which we call IRAKIMiDs, with a unique profile that combines the activity of IRAK4 degradation and immunomodulatory imide drugs, or IMiDs, for the treatment of MYD88-mutated diffuse large B-cell lymphoma, or DLBCL. In oncology, IRAK4 is an obligate protein in MYD88 signaling and this activated mutation is well characterized to drive oncogenesis. IMiDs are a class of drugs that degrade zinc-finger transcription factors, such as Ikaros and Aiolos, resulting in the restoration of Type 1 interferon, or Type 1 IFN, signaling pathway which is relevant in treating lymphoma. Our IRAKIMiDs combine the activity of the IMiDs with IRAK4 degradation in a single agent and address both the IL-1R/TLR and the Type 1 IFN pathways synergistically and in doing so demonstrate broad activity against MYD88-mutant lymphomas. We believe this will be the first precision medicine in lymphoma to target a genetically defined population, which accounts for 25% to 30% of DLBCL patients. We have observed that the functional synergy between the degradation of IRAK4 and IMiD activity results in broad activity against MYD88-mutant lymphomas *in vitro* and in mouse xenograft models, leading to rapid, complete and sustained tumor regressions, even when dosed intermittently. In the third quarter of 2020, we declared KT-413 as a development candidate and initiated IND-enabling activities. We expect to file an IND in the second half of 2021 and, if cleared, to begin a Phase 1 clinical trial thereafter.

We are developing our selective STAT3 degraders for the treatment of hematological malignancies and solid tumors, as well as autoimmune diseases and fibrosis. STAT3 is a transcription factor activated through a variety of different cytokine and growth factor receptors via janus kinases, or JAKs, as well as through oncogenic fusion proteins and mutations in STAT3 itself. We believe the diverse functions of STAT3 in tumor biology, evasion of immune surveillance by tumor cells, and inflammation and fibrosis provide opportunities to address a wide variety of high unmet need disease indications through the targeting of a single genetically and clinically validated pathway. While the JAK-STAT pathway has been partially addressed with several clinically successful JAK-targeting agents, we believe there are currently no drugs that specifically affect STAT3 broadly across all the relevant cell types. Small molecule STAT3 dimerization inhibitors targeting the SH2 domain have been in development, but significant challenges remain: first, homology of SH2 domains among all STAT family members impacts the ability to achieve specificity for STAT3, and second, inability to block dimerization independent transcriptional activities of STAT3. For these reasons, we believe that STAT3 degraders may provide a transformative solution to the development of targeted and selective drugs to address multiple STAT3 dependent pathologies. We recently nominated KT-333 as a STAT3 development candidate for liquid and solid tumor indications, and we expect to submit an IND to the FDA in the fourth quarter of 2021 and if cleared, initiate a Phase 1 trial thereafter.

Our Pegasus™ Platform

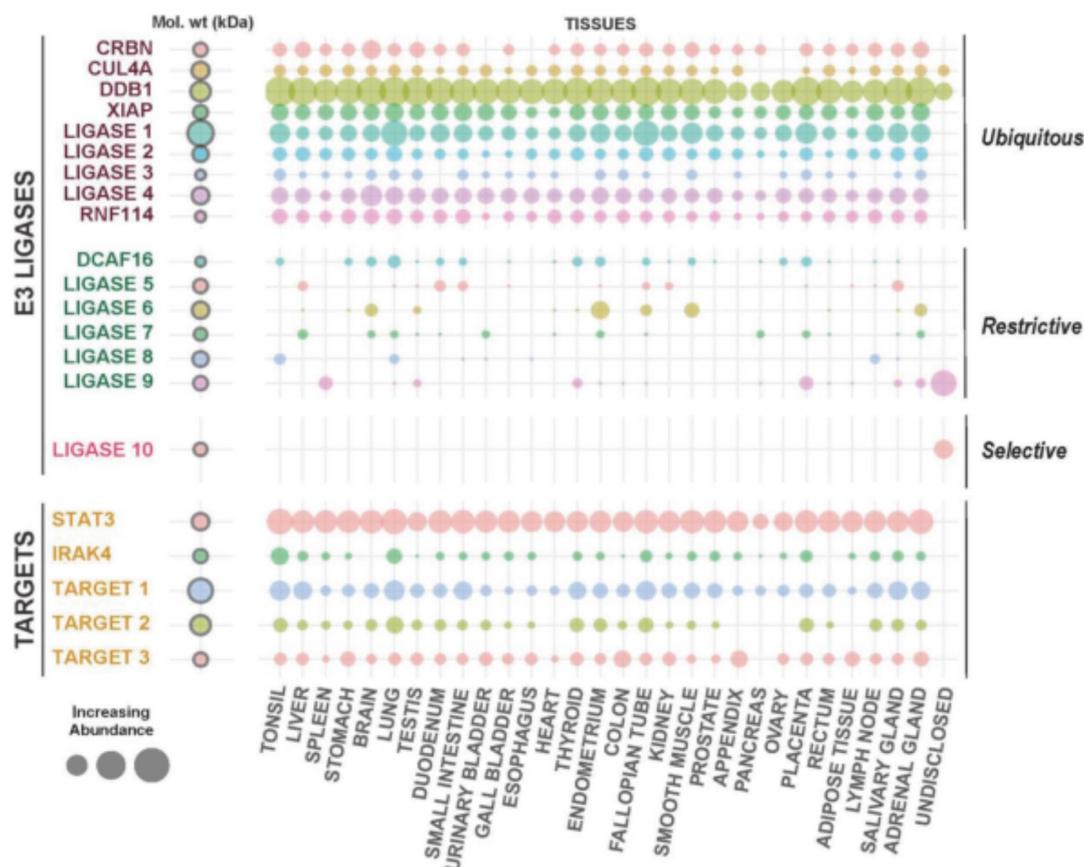
We built Pegasus™, our proprietary TPD platform, to serve as an effective drug discovery and development engine leveraging our proprietary expertise and knowledge, as well as numerous chemistry, biology and computational capabilities. Our platform allows us to discover highly efficient and selective degraders by matching the right target with the ideal E3 ligase and optimizing molecular properties in order to increase the likelihood of therapeutic success for a particular disease state. Pegasus™ also allows us to design degraders with the appropriate pharmaceutical properties through our ability to study and model ternary complexes. We believe our understanding of degradation profiles across multiple tissues and cell types in different species increases the probability of clinical translation success. We believe our TPD platform is an engine for innovation, allowing us to expand the druggable proteome and thereby access critical disease pathway nodes that have to date been considered either undruggable or inadequately addressed with conventional modalities. Our capabilities have been developed through the key features of our Pegasus™ platform, which include the following:

- **E3 Ligase Whole-Body Atlas**
- **E3 Ligase Binders Toolbox**
- **Ternary Complex Modeling**
- **Quantitative System Pharmacology Model**
- **Proprietary Chemistry**

E3 Ligase Whole-Body Atlas. We have developed a proprietary human whole body E3 Atlas for mapping expression patterns of all known human E3 ligases in both disease and healthy contexts by combining the power of quantitative, high-resolution proteomics with proprietary algorithms. We are refining the characterization of the expression profiles in healthy and diseased tissues of generally well-established liganded E3 ligases like cereblon and VHL and, more importantly, of the approximately 600 naturally-occurring E3 ligases, most of which are still unliganded. We are establishing subcellular localization indices for each E3 ligase and determining their absolute abundances. We believe our approach overcomes the limitations of relying on publicly available RNA or antibody-based protein expression datasets, which often lead to inaccuracies in determining relative E3 ligase expression levels in different biological contexts.

Our proprietary E3 Ligase Whole-Body Atlas enables data-driven disease-selective protein degradation strategies based on all of the mapped E3 ligases, which we view as a paradigm shift from relying on the limited number of E3 ligases typically exploited for TPD and provide us with a distinct competitive advantage. Using comparative analyses of expression patterns, we can identify selective pairings of E3 ligases with therapeutic targets of interest, including tissue-selective or tissue-restrictive pairings. We believe this approach is central to building out a toolbox of differentiated E3 ligase binders. Furthermore, we are able to use our custom-built Quantitative Systems Pharmacology Models in combination with proprietary data on the absolute abundance of E3 ligases and targets to predict cellular efficacy. The graph below shows an example of diverse expression profiles, using circle size as a relative abundance measure, for E3 ligases and selected targets across a panel of healthy tissues (on the x-axis), taken from our proprietary E3 Ligase Whole-Body Atlas.

Figure 4. Example of Diverse Expression Profiles for Selected Targets and E3 Ligases Across a Panel of Healthy Tissues, Taken from Our Proprietary E3 Ligase Whole-Body Atlas.



E3 Ligase Binders Toolbox. Leveraging the knowledge generated by our E3 Ligase Whole-Body Atlas, we are building a proprietary toolbox of differentiated E3 ligase binders for the development of next-generation targets and disease-specific degraders. We are focused on building an expanded library of E3 ligases and novel ligands with differentiated expression profiles in order to selectively pair them with targets in specific tissues, cell types and subcellular compartments. We believe that this approach to degrader design will lead to more selective target degradation in disease contexts, while avoiding target degradation in tissues associated with known toxicities, which we believe will lead to a substantially improved overall safety profile for our degrader molecules. Through our knowledge of E3 ligases and proprietary data on expression profiling, we believe we are uniquely positioned to identify both differentiated and ligandable E3 ligases that can be deployed against multiple targets, spanning broad therapeutic areas.

Ternary Complex Modeling. We believe that the understanding of the activity of the ternary complex is critical to the optimization and development of our degrader therapeutics. Ternary complexes are formed when a degrader binds to both an E3 ligase and the protein of interest. We characterize this interaction with both structural biology and biophysical techniques and utilize a sophisticated, structure-based approach to modeling. Our proprietary approach is tailored to the unique features of heterobifunctional degraders, which, unlike small-molecule inhibitors, facilitates proximity-based engagement of an E3 ligase with a target protein. Design of degraders requires consideration of both the length and composition of the linker, which can have a significant impact on the formation of the ternary complex and ultimately the efficiency of the degradation. We have developed and fully integrated into our discovery platform an efficient and powerful Ternary Complex Modeling, or TCM, method. The TCM method combines computational evaluation of tens of millions of potential protein-protein complexes, leveraging cloud computing resources, with statistical analyses to establish optimal linker lengths and geometry and to predict key aspects of target/degrader/E3 ligase ternary complexes. Our approach allows for rapid design of degraders, which in combination with design-build-test cycles, allows us to optimize our degraders by identifying key interactions and geometric constraints.

Quantitative Systems Pharmacology Model. Our proprietary Quantitative Systems Pharmacology, or QSP, model helps solve the complex equations required in TPD to accurately translate PK/PD into optimal human dosing. Our QSP model enables us to refine the understanding of each parameter that impacts the protein degradation profiles of degraders in tissues and then predict these varying parameters in different contexts. These parameters can include the affinity of binding to proteins and E3 ligases, ternary complex kinetics, protein half-life, target protein and E3 ligase concentrations. Using data from our proprietary E3 Ligase Whole-Body Atlas, combined with relevant biochemical and cellular degradation assays, we deploy the model to enhance optimal target and E3 ligase selection. QSP modeling is able to predict how the relative concentrations of the E3 ligase and the target protein impact the maximal degree of degradation and can be used to exclude E3 ligases whose concentration in target tissues may be insufficient to achieve the desired level of degradation. Our model is able to predict the impact of differential targeting versus E3 ligase expression profiles on degradation efficiencies. These insights are taken into consideration in the selection of the optimal E3 ligase for the target of interest to achieve the desired degradation profile whether it is systemic or restricted degradation across different cell types.

Proprietary Chemistry. We are leveraging our experienced team of dedicated scientists and experts with decades of experience in chemistry, structural biology and computational chemistry to optimize both E3 binders and target protein binders to convert them into highly efficient and selective degraders. We deploy diverse compound and virtual libraries for identification of starting ligands that bind to both the E3 ligase of interest and target. Our curated libraries include compounds with preferred physicochemical properties conducive to achieving oral bioavailability, and incorporate both covalent and non-covalent chemical scaffolds, as well as DNA-encoded libraries. We deploy direct-affinity assays and bead-based separation for fragment-based and DNA-encoded library screening. Computational chemistry is used to find suitable binding pockets to enable virtual screening. These *in silico* exercises rely upon structural biology, and together enable structure-based drug discovery. To support rapid synthesis of degrader molecules, we have built our own readily accessible and diverse library of linkers to connect binders to the E3 ligase and the target. We then integrate our TCM capabilities with proprietary linker chemistry to enable rational degrader design and optimization, reducing the time to development of highly efficient and selective degraders with the pharmaceutical properties tailored to specific patient populations and diseases. In this way, we were able to develop second-generation molecules with significantly improved permeability and bioavailability while sustaining the strong degrader properties exhibited in our first-generation molecules.

Our Programs

IRAK4 Degradation for IL-1R/TLR-driven Immunology-inflammation Diseases

Summary

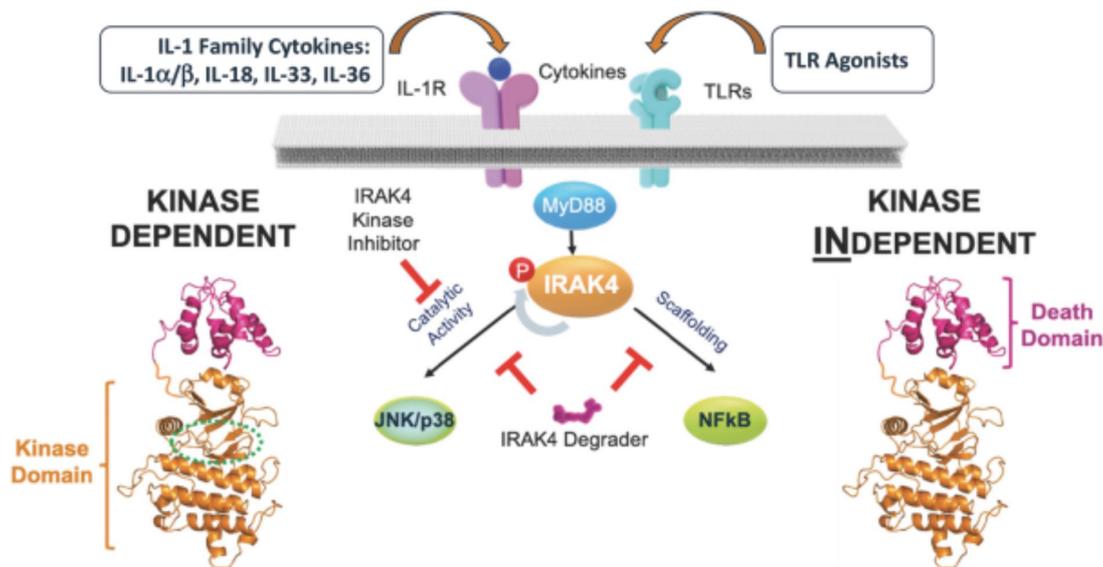
We are developing KT-474, a highly active and selective, orally bioavailable IRAK4 degrader, for the treatment of IL-1R/TLR-driven immune-inflammatory conditions and diseases with high unmet medical need, including HS, AD and rheumatoid arthritis, or RA. We have chosen to pursue IRAK4 degradation due to the well-validated role of the IL-1R/TLR pathway in immunology and inflammation and the potential advantage that drugging a single node of multiple different mediators of inflammation has over other approaches focused on targeting one of many cytokines that stimulate the IRAK4 node. IRAK4 is a critical node in the IL-1R/TLR signaling pathway, which is dependent on both IRAK4's kinase activity and scaffolding function. We have demonstrated through our *in vitro* and *in vivo* studies that KT-474 induces IRAK4 degradation, impacting both the kinase and the scaffolding functions, and therefore can selectively block IL-1R/TLR-mediated inflammation in a way we believe to be superior to IRAK4 kinase inhibitors. We therefore believe KT-474 has the potential to improve outcomes over current treatment options as well as other drugs currently in development. In December 2020, we submitted an IND for KT-474 to the FDA, and in February 2021 we initiated dosing in a Phase 1 trial evaluating KT-474. In July 2020, we announced a strategic collaboration with Sanofi to develop and commercialize therapies targeting IRAK4 in patients with immune-inflammatory diseases. See the section entitled "Business—Collaborations—Collaboration Agreement with Genzyme Corporation" appearing elsewhere in this Annual Report for more information.

IRAK4 is a key component of the myddosome, a multiprotein complex involved in innate immunity that mediates signaling through TLRs and IL-1Rs. The IRAK4 protein is ubiquitously expressed across multiple different tissue types, including skin, lymphoid tissue, bone marrow, gastrointestinal tract, and lung.

The function of IRAK4 is dependent both on its kinase activity and on its scaffolding function, which are required for the assembly of the myddosome complex following TLR or IL-1R engagement and MYD88 activation. While the kinase function is primarily responsible for the phosphorylation events in the IRAK4-JNK axis, the scaffolding function is primarily responsible for the NF-KB activation and downstream gene traction of several key pro-inflammatory cytokines and chemokines.

We believe IRAK4 degradation is superior to IRAK4 kinase inhibition as our preclinical data suggests that it is critical to block both the kinase activity and scaffolding functions of the IRAK4 protein, which requires removal, as opposed to just inhibition, of the protein. IL-1 family cytokines, including IL-1a, IL-1 β , IL-18, IL-36, and IL-33, have been implicated in a variety of different immunology-inflammation conditions and diseases. As both TLRs and IL-1Rs are involved in the production and response to all of these IL-1 family cytokines, IRAK4 targeting with a single small molecule degrader could impact multiple different cytokines and chemokines and thereby provide a transformative approach to the treatment of IL-1R/TLR-driven diseases.

Figure 5. IRAK4 Function is Comprised of Both Kinase-Dependent and -Independent Activity.



Non-Interventional Trial evaluating IRAK4 expression in HS and AD patients

In October 2020, we announced interim data from a non-interventional trial evaluating IRAK4 expression in the skin and blood of patients with HS and AD, as well as the effect of KT-474 on IRAK4 levels in peripheral blood mononuclear cells (PBMC) following *ex vivo* treatment. The goal of conducting a non-interventional study in HS and AD is to understand IRAK4 expression in diseased tissues and demonstrate *ex vivo* proof of mechanism with KT-474 in patients prior to conducting our clinical trials. The non-interventional trial was designed to enroll up to 30 patients with mild, moderate and severe HS and up to 10 patients with moderate or severe AD. The interim data from HS patients were presented at the 5th Annual Symposium on Hidradenitis Suppurativa Advances (SHSA).

IRAK4 levels were measured in skin biopsies obtained from lesional, peri-lesional and non-lesional skin and in blood from HS patients. The effect of KT-474 or an IRAK4 kinase inhibitor on IRAK4 levels were measured following *ex vivo* incubation of whole blood. Interim results showed:

- IRAK4 expression can be quantified in the skin using immunofluorescence and mass spectrometry, and in PBMC by flow cytometry.
- IRAK4 expression in the skin was higher in lesional and peri-lesional skin compared to unaffected skin (see Figure 6).
- IRAK4 was detected in the blood across all PBMC subsets, with the highest expression in monocytes.
- *Ex vivo* treatment of whole blood with KT-474 substantially lowered IRAK4 levels across all PBMC subsets in the blood, whereas *ex vivo* treatment with an IRAK4 kinase inhibitor increased IRAK4 levels in T and NK cells (see Figure 7).

Figure 6: IRAK4 Expression in Skin of HS Patients, as Quantified by Immunofluorescence and Mass Spectrometry

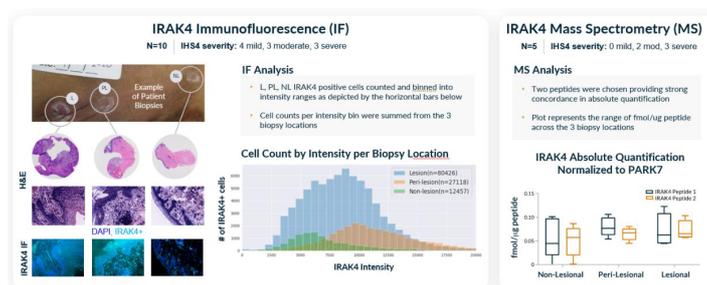
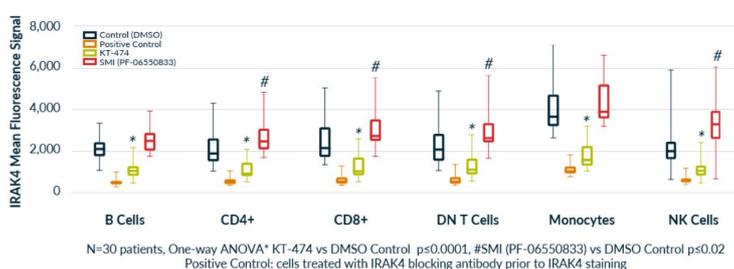


Figure 7: IRAK4 Levels in PBMC Subsets Following Treatment with IRAK4 Degradator or Kinase Inhibitor



These data support the relevance of the IRAK4 signaling pathway in HS and provide *ex vivo* proof of mechanism for KT-474 in PBMC of HS patients. We expect to present final results from the non-interventional trial, including additional data in HS patients as well as in AD, in the second quarter of 2021.

In July 2020, we announced a strategic collaboration with Sanofi to develop and commercialize therapies targeting IRAK4 in patients with immune-inflammatory diseases. See the section entitled “Business—Collaborations—Collaboration Agreement with Genzyme Corporation” appearing elsewhere in this Annual Report for more information.

Development Opportunities and Differentiation from IL-1 Family Cytokine Antibodies

There are numerous cutaneous, rheumatic and gastrointestinal immunology-inflammation disease indications for which pathogenesis involves IL-1 family cytokines as well as TLR stimulation. These present opportunities where we believe a highly efficient and selective IRAK4 degrader would provide significant advantages over both currently approved treatment options and those in clinical development. We are initially prioritizing indications such as HS, AD, and RA where there is clinical proof of concept for targeting cytokines impacted by the IL-1R/TLR pathway but for which there continues to be a high level of unmet need.

Hidradenitis Suppurativa

HS is a chronic, destructive, painful and debilitating inflammatory skin disease affecting up to 1% of both the U.S. and global population. Patients with HS have numerous painful, draining nodules and abscesses, usually within skin folds, that are characterized by inflammation and bacterial colonization. Currently HS is treated symptomatically with corticosteroids, antibiotics and surgery. The only FDA-approved treatment for HS is the anti-TNF antibody adalimumab, which provides some benefit to approximately 50% of patients with moderate-to-severe disease but is not curative. Thus, there remains a high unmet need for better therapies for the treatment of HS.

Bacterial activation of TLRs, as well as the production of IL-1a, IL-1 β , and IL-36 by keratinocytes and inflammatory cells leading to inflammation characterized by high levels of TNF-a, IL-6, and IL-17, are central to the pathogenesis of HS. Monoclonal antibodies targeting individual cytokines such as IL-1a (bermekimab), IL-1a/ β receptor (anakinra), and IL-17 (secukinumab and bimekizumab) have shown preliminary clinical activity in HS and provide clinical validation for targeting the IL-1R/TLR pathway in HS. As such, an IRAK4 degrader which acts on multiple cytokines as well as TLRs has the potential to offer a significant advantage over the single-cytokine-targeting agents currently being developed.

Atopic Dermatitis

AD is a chronic, pruritic inflammatory skin disease that occurs most frequently in children but also affects adults. In the U.S., the prevalence of AD is approximately seven to ten percent. AD follows a chronic relapsing course over month to years, with dry skin and severe pruritus as the primary symptoms, sometimes accompanied by skin thickening from chronic scratching and fissuring. AD is treated symptomatically with topical therapies, including emollients, corticosteroids, and phosphodiesterase inhibitors. The lone FDA-approved systemic treatment is the IL-4Ra targeting antibody dupilumab, though only approximately 40% of moderate-to-severe disease patients met the primary endpoint in its Phase 3 trials, leaving a significant percentage of patients who are currently underserved.

Furthermore, there is evidence that IL-33 and IL-1 are both involved in the generation of inflammation in both AD and other allergic diseases, including eosinophilic asthma and chronic rhinosinusitis. Single-cytokine-targeting monoclonal antibodies against IL-33 (etokimab) and IL-1a (bermekimab) have shown preliminary clinical activity in AD. Thus, the ability of an IRAK4 degrader to impact the production of both IL-33 and IL-1, through complete TLR signaling blockade, and the cellular response to both cytokines, through complete IL-1R signaling blockade, provides a compelling mechanistic rationale for development in AD.

Rheumatoid Arthritis

RA is the most common inflammatory arthritis, affecting approximately 0.5% of the U.S. population. The synovial inflammation characteristic of RA is driven by Th1 and Th17 immune responses with production of TNF-a and IL-1 family cytokines, including IL-1, IL-18 and IL-33, IL-6 and IL-17. Multiple therapies targeting the IL-1R/TLR pathway are approved for RA, and recently an IRAK4 kinase inhibitor (PF-06650833) has shown clinical activity comparable to the JAK inhibitor tofacitinib and a favorable safety profile in a randomized, placebo-controlled Phase 2b study in RA patients with inadequate response to methotrexate. Based on these early signs of activation, we believe a degrader-based approach which impacts both the kinase activity and the scaffolding function of IRAK4 may have the potential for a more transformative effect on the disease.

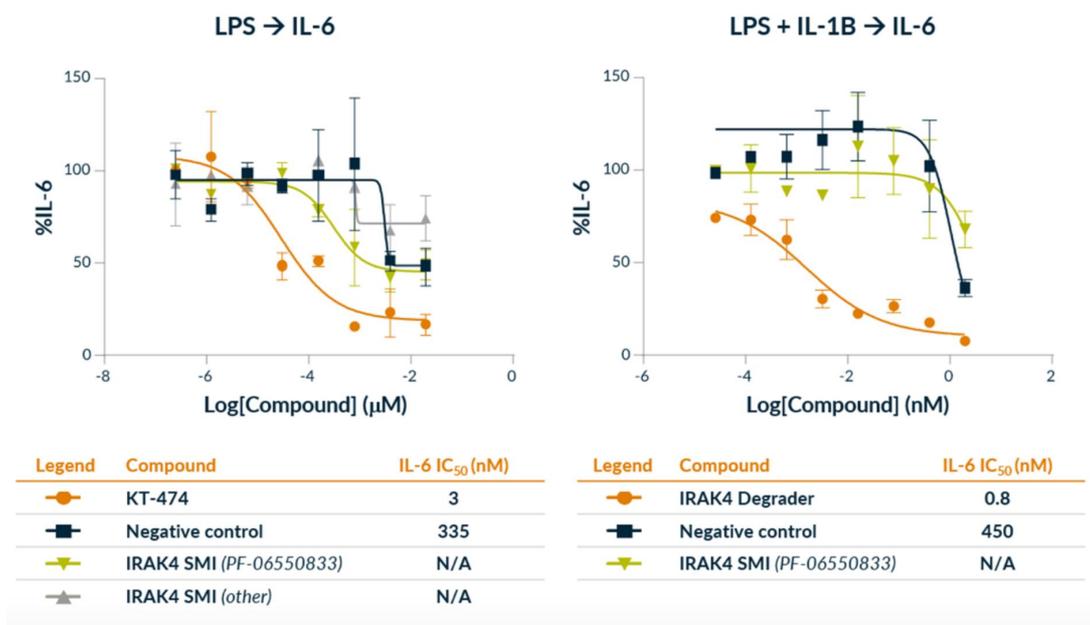
Preclinical Studies and Data

In support of our IND-enabling studies, we have demonstrated KT-474's high activity, selectivity and therapeutic potential in both *in vitro* and *in vivo* studies.

Stimulation and Comparison to IRAK4 Kinase Inhibitors

We assessed the functional activity of KT-474 by measuring pro-inflammatory cytokine levels upon activation. Cells were pretreated with KT-474, a negative control, and small molecule IRAK4 kinase inhibitors. The figure below shows KT-474 is better able to inhibit IL-6 under both LPS and LPS + IL-1B than clinically active IRAK4 small molecule kinase inhibitors.

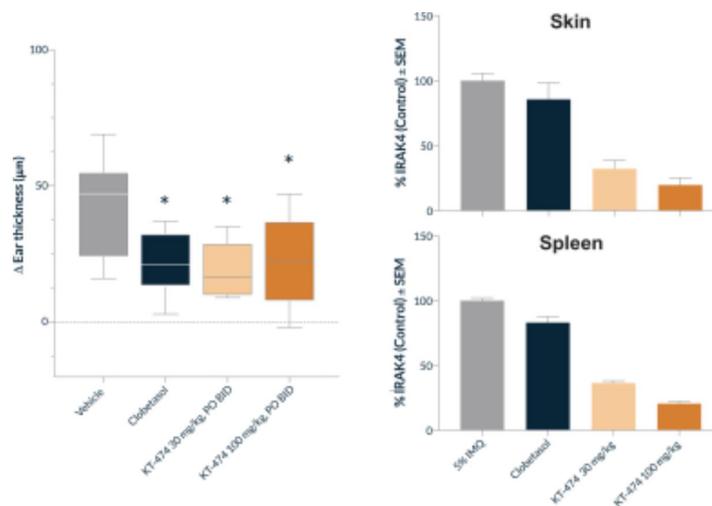
Figure 8. IRAK4 Degradation Superior to Kinase Inhibition in Cytokine Production



In Vivo Data

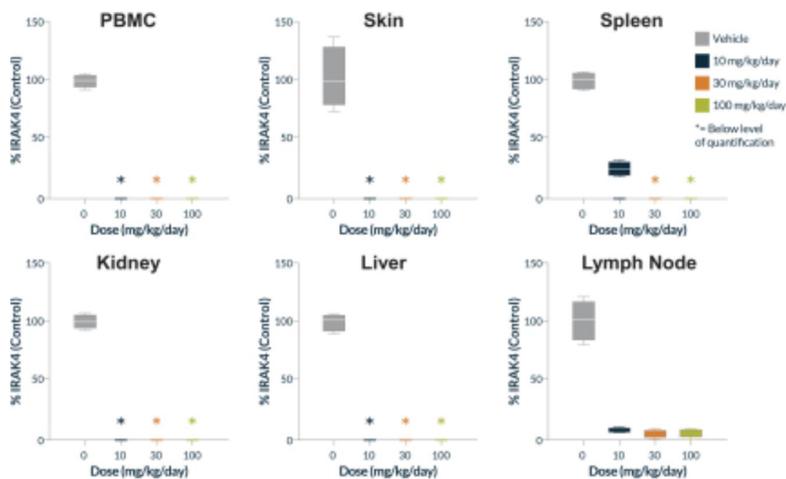
Topical application of the TLR7/8 agonist, imiquimod, or IMQ, induces skin thickening associated with inflammatory cell infiltration, activates the NF-κB pathway and IL-23/IL-17 axis, and produces IL-1 family cytokines from keratinocytes, recapitulating several key pathological features of skin inflammation, including HS and psoriasis. In this *in vivo* model, orally administered KT-474 inhibited topical IMQ-induced skin thickening, which was a reflection of local and systemic inflammation, to an extent comparable to a topical corticosteroid (clobetasol) at doses achieving at least 60-70% IRAK4 knockdown in skin and spleen (Figure 9).

Figure 9. KT-474 Downregulates IRAK4 Expression and Inhibits Skin Thickening in Mouse Imiquimod Model of Psoriasis.



In a 14-day non-GLP toxicology study of daily, orally-administered KT-474 in rats and non-rodents, the compound was well-tolerated at doses of up to 600 mg/kg in rats and 100 mg/kg in non-rodents. Notably, pharmacodynamic assessment demonstrated complete knockdown of IRAK4 24 hours after the last dose on day 15 in multiple tissues including skin, spleen, lymph nodes and animal peripheral blood monocytes, PBMCs, as shown in Figure 10. Together this demonstrates that nearly complete systemic degradation of IRAK4 was well-tolerated and supported the advancement of KT-474 into further development.

Figure 10. IRAK4 Knockdown in Tissues After 14 Days of KT-474 Dosing in Non-Rodent Non-GLP Toxicology Study.



In addition, the reversibility of IRAK4 knockdown *in vivo* was demonstrated in mice and non-rodents, where recovery of IRAK4 levels in blood (PBMC) and skin was observed within 48 to 72 hours following cessation of daily oral dosing. We believe these data point to a potential safety advantage for TPD relative to genetic medicines approaches of protein knockdown, as cessation of the TPD agent is sufficient to restore protein levels back to steady state within a reasonable timeframe.

In summary, these preclinical data show that orally administered KT-474 safely and selectively suppresses IRAK4 expression in rodents and non-rodents, inhibits inflammation, including neutrophil infiltration, in murine models mechanistically relevant to the pathogenesis of HS, AD, and RA and potentially other diseases, and demonstrates a therapeutic advantage of IRAK4 degradation over IRAK4 kinase inhibition.

Clinical Development Plan

In December 2020 we submitted an Investigational New Drug Application, or IND, to the U.S. Food and Drug Administration, or FDA, for KT-474, and in February 2021 we initiated the SAD portion of our Phase 1 trial in adult healthy volunteers. This is the first time that a heterobifunctional small molecule degrader has been administered to healthy volunteers in a placebo-controlled, randomized clinical trial. In the second half of 2021, we expect to initiate enrollment in the MAD portion of the Phase 1 trial of KT-474, including healthy volunteers and a subsequent cohort of HS and AD patients, pending FDA's removal of the partial clinical hold for this portion of the trial.

The primary endpoints of the Phase 1 trial are to determine the safety and tolerability of KT-474 when administered as daily oral doses at escalating dose levels. Secondary endpoints will include characterization of the pharmacokinetic and pharmacodynamic profiles of multiple doses of KT-474 over an established timeframe.

Pharmacodynamic endpoints to demonstrate proof of mechanism and proof of biology will include IRAK4 levels in blood and skin, levels of pro-inflammatory cytokines in *ex vivo* stimulated PBMC, and plasma levels of high sensitivity C-reactive protein. We plan to also characterize the pharmacokinetic and pharmacodynamic profile of the recommended Phase 2 dose of KT-474 in an additional cohort of up to 20 AD and HS patients before initiation of Phase 2 studies. We expect that the combination of safety, pharmacokinetic and pharmacodynamic endpoints, including PK/PD relationships, will inform selection of one or more predicted-effective doses to take into subsequent proof of concept trials in our prioritized indications. Phase 2 randomized placebo-controlled trials are expected to be conducted in one or more indications including but not limited to AD, HS, and RA.

Summary

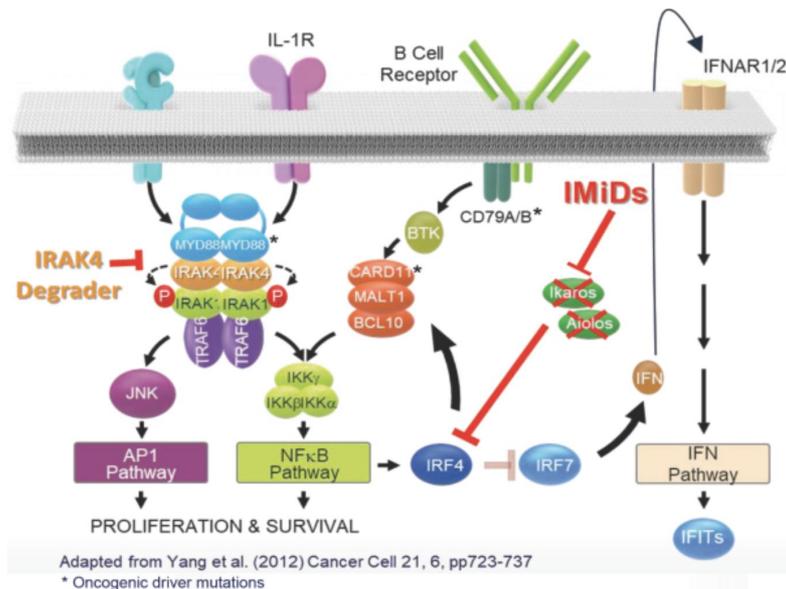
We are developing another group of IRAK4 degraders, which we call IRAKIMiDs, with a unique profile that combines the activity of IRAK4 degradation and IMiDs for the treatment of MYD88-mutated DLBCL. In oncology, IRAK4 is an obligate protein in MYD88 signaling and this activated mutation is well characterized to drive oncogenesis. IMiDs are a class of drugs that degrade zinc-finger transcription factors, such as Ikaros and Aiolos, resulting in the restoration of Type 1 IFN signaling pathway which is relevant in treating lymphoma. Our IRAKIMiDs combine the activity of the IMiDs with IRAK4 degradation in a single agent and address both the IL-1R/TLR and the Type 1 IFN pathways synergistically with a goal of demonstrating broad activity against MYD88-mutant lymphomas. We believe this will be the first precision medicine in lymphoma to target a genetically defined population, which accounts for at least 25% of DLBCL patients. We have observed the degradation of IRAK4 and IMiD activity results in additivity and synergy *in vitro*. IRAKIMiDs combine both of these mechanisms in a single compound. Our IRAKIMiD degrader, KT-413, has demonstrated broad activity against MYD88-mutant lymphomas *in vitro* and in mouse xenograft models, leading to rapid, complete and sustained tumor regressions, even when dosed intermittently. During the third quarter of 2020, we declared KT-413 as our development candidate for our IRAKIMiD program, and we expect to submit an IND to the FDA in the second half of 2021 and, if cleared by the FDA, initiate a Phase 1 trial thereafter.

Target Rationale and Mechanism of Action

In DLBCL, the activating mutation of MYD88 drives activation of the NF- κ B transcription factor and pro-survival mechanisms such as IRF4. MYD88 is a protein that forms a multiprotein signaling complex, known as the myddosome, which transduces receptor agonism from both the TLR and IL-1 b receptors. IRAK4 is an integral component of the myddosome, and both its catalytic kinase activity as well as its scaffolding function are required to drive downstream signals from the myddosome.

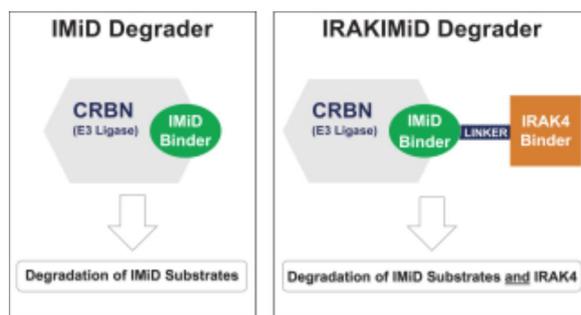
The constitutive activation of NF- κ B is a hallmark of several B-cell lymphoma subtypes. In DLBCL, NF- κ B activation is driven by a range of oncogenic alterations in several upstream pathways and regulators. Multiple co-mutations in these complexes often occur within the same tumor, emphasizing the dependence of these cancers on NF- κ B activation. IMiDs such as lenalidomide drive a partial downregulation of NF- κ B and IRF4, resulting in the restoration of Type 1 IFN signaling and promoting cell death.

Figure 11. NF- κ B is Activated by Complimentary Mechanisms in Diffuse Large B Cell Lymphoma.



Leveraging knowledge and chemistry expertise derived from the design of our selective IRAK4 degrader program, we have designed a novel class of heterobifunctional IRAK4 degraders, which we call IRAKIMiDs, that utilize an active IMiD as the cereblon binder to simultaneously engage and degrade both IRAK4 and IMiD substrates, such as Ikaros and Aiolos, thus combining the activity of two molecules in a single agent. IRAKIMiDs therefore combine two highly relevant therapeutic mechanisms in a single compound, enabling the functional synergy of NF- κ B inhibition and upregulation of the Type 1 IFN response that results in increased and broader single-agent activity in MYD88-mutated DLBCL as compared to either mechanism alone.

Figure 12. IRAKIMiDs (right) Combine Both IRAK4 Degradation and IMiD Activity in a Single Agent.



Pre-IND Status and Next Steps

KT-413, our development candidate in our IRAKIMiD program, is currently in preclinical development, and we expect to file an IND with the FDA in the second half of 2021 and, if cleared, initiate a Phase 1 trial thereafter. Our planned Phase 1a trial is expected to include dose escalation and will assess safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary clinical activity in patients with B-cell lymphomas, including MYD88-mutant and -wild type DLBCL, leading to selection of the dose and schedule to take into Phase 1b. The Phase 1b expansion cohorts are expected to assess safety and clinical efficacy in MYD88-mutant versus MYD88-wild-type DLBCL, as well as Waldenström's macroglobulinemia, and other MYD88MT NHL subsets. We are also planning expansion into other tumors sensitive to IL-1R/TLR targeting.

Development Opportunities and Differentiation of Novel Therapies in MYD88-Mutated DLBCL

Oncogenic mutations of MYD88, most commonly MYD88L265P, are common in several subsets of DLBCL. In particular, MYD88 is estimated to be mutated in approximately 30-40% of activated B cell DLBCL, or ABC-DLBCL, cases, 30-80% of primary CNS lymphoma cases, and 45-75% of primary extranodal lymphomas cases. In addition, MYD88 is mutated in approximately 90% of Waldenström macroglobulinemia cases. The presence of MYD88 mutations in DLBCL is often associated with poorer response to chemotherapy and reduced overall survival compared to other genetic subtypes, supporting the need for more effective therapies targeting MYD88-mutated DLBCL.

Front-line treatment of DLBCL typically involves the R-CHOP treatment regimen of chemotherapy combined with rituximab. While effective in many other patients, front-line chemotherapy has significantly poorer survival rates in DLBCL subsets where MYD88 mutations are prevalent. In additional lines of therapy, several novel targeted therapies have been approved recently, including the combination of polatuzumab, bendamustine and rituximab, as well as CD19-targeting chimeric antigen receptor T-cells. While these agents have some notable activity, many patients fail to respond to or subsequently relapse from these therapies, with no adequate treatment options. Several targeted therapies that impact the NF- κ B pathway, such as the Bruton's tyrosine kinase inhibitor ibrutinib, or the IMiD lenalidomide, have shown modest single agent activity, with poor durability of response in MYD88-mutated DLBCL.

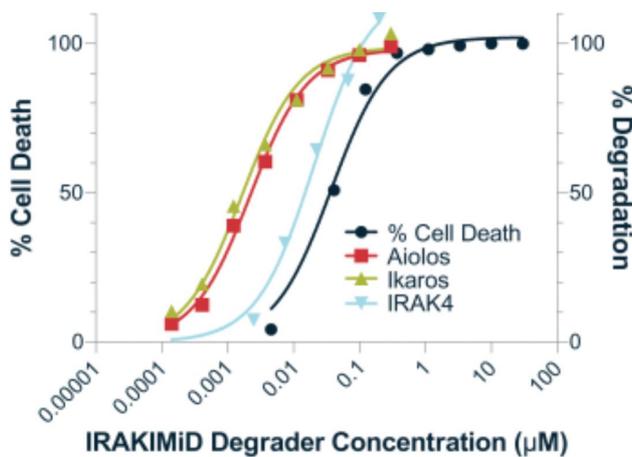
Based on our preclinical data, we believe KT-413, which synergistically combines the activity of both IRAK4 and IMiD substrate degradation to exploit complimentary pathway signaling, will have the potential to improve upon the efficacy of IRAK4 kinase inhibitors and other therapies, including BTK inhibitors and IMiDs, and provide single-agent activity in MYD88-mutated DLBCL.

In support of our preclinical development, we have demonstrated our IRAKIMiD degraders' high selectivity and therapeutic potential in both *in vitro* and *in vivo* studies.

To assess the activity of our IRAKIMiD degraders in both MYD88-mutated and -wild-type cell lines, we conducted various *in vitro* studies in a panel of cell lines. MYD-88-mutated cell lines included ABC-DLBCL lines such as OCI-Ly10, SUDHL2, and TMD8 while MYD-88-wild-type cell lines included OCI-Ly19, U2932, and SUDHL6. We have shown that IRAK4 degradation, as opposed to IRAK4 inhibition, shows additivity and synergy when combined with IMiDs *in vitro*. Specifically, combining an IRAK4 degrader with the IMiD pomalidomide shows additive and synergistic activity in several MYD88-mutated cell lines *in vitro*, supporting the combined effect of targeting both the MYD88 and IRAK4 pathways together. Notably, we did not see an additive effect when IRAK4 kinase inhibitors were combined with IMiDs, suggesting that the greater activity of IRAK4 degradation is needed for synergistic activity. We believe these data support the development of our unique class of degraders, which we call IRAKIMiDs.

To characterize the relationship between cell killing activity and the pharmacodynamic effect of an IRAKIMiD degrader, we measured protein levels of IRAK4, Ikaros and Aiolos in OCI-Ly10 cells after 24 hours of drug exposure. As shown in Figure 13, treatment with an IRAKIMiD degrader resulted in significant degradation of each of IRAK4, Ikaros, and Aiolos. Moreover, the degree of target protein degradation was strongly associated with the degree of cell killing, providing proof of concept that dual targeting of IRAK4 and IMiD substrates is capable of strongly affecting tumor biology in MYD88-mutated DLBCL.

Figure 13. Pharmacodynamic Analysis of IRAK4, Ikaros, and Aiolos in the MYD88MT Cell Line OCI-Ly10 Treated with an IRAKIMiD Degradation. Degree of Cell Killing Activity is Strongly Associated with the Degree of Degradation of Both IRAK4 and IMiD Substrates.



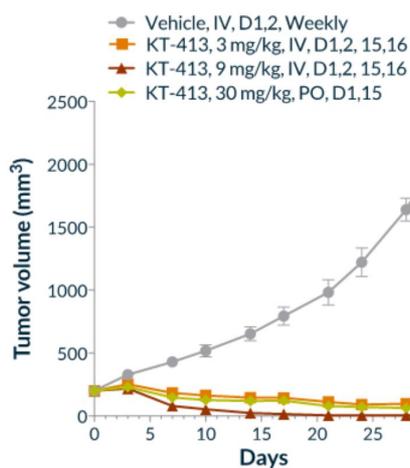
KT-413 is a selective and efficient degrader of both IRAK4 (DC50 = 8nM) and the IMiD substrates Ikaros and Aiolos (DC50 = 2nM) and shows activity in a range of MYD88-mutated cell lines, including OCI-Ly10, TMD8 and SUDHL2, irrespective of other co-mutations, as shown in Figure 14. Notably, KT-413 is significantly less active in MYD88-wild-type cell lines, including U2932 and OCI-Ly19, supporting the potential for targeting tumors harboring MYD88 mutations.

Figure 14. KT-413 Degradation is Significantly More Active in MYD88MT versus MYD88WT Cell Lines.

MYD88	Cell Line	Co-mutations	Cell (IC ₅₀ nM)
mut	OCI-LY10 CTG IC ₅₀ (nM)	CD79A	7
mut	SU-DHL2 CTG IC ₅₀ (nM)	TNFAIP3, IRF4, BCL6	14
mut	TMD8 CTG IC ₅₀ (nM)	CD79A, IRF4	29
Wild type	OCI-LY19 CTG IC ₅₀ (nM)	None	3,400
Wild type	U2932 CTG IC ₅₀ (nM)	BCL6	2,600

To assess the *in vivo* activity of KT-413, we used a MYD88MT OCI-LY10 xenograft mouse model. Mice were administered KT-413 orally or parenterally on an intermittent schedule every 3rd or 4th day and monitored for tumor volume over time. As shown in Figure 15, KT-413 induced tumor responses and complete regressions when given under either an oral, or PO, or intravenous, or IV, administration and under an intermittent schedule. Tumor responses were durable, maintaining regression for upwards of 4 weeks past the last dose, suggesting that infrequent dosing may be adopted with this mechanism with little impact on potential for activity.

Figure 15. KT-413 Induced Strong and Durable Regressions on Intermittent PO or IV Dosing in OCI-Ly10 Xenograft Tumors.

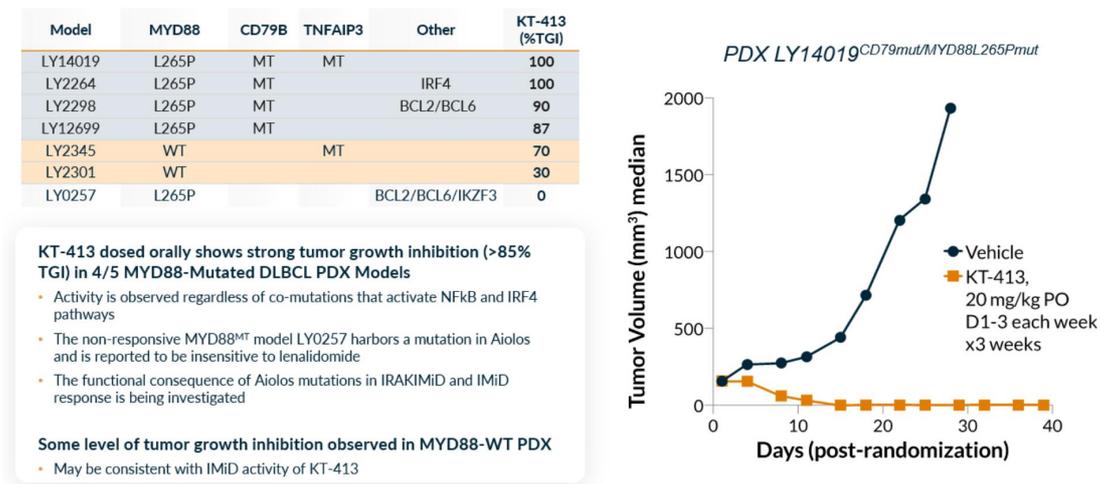


Dose	Schedule	D21 TGI
3 (IV)	D1,2	94%
9 (IV)	QW	99%
3 (IV)	D1,2	95
9 (IV)	Q2W	99%
12 (IV)	D1	99%
30 (PO)	Q2W	96%

>90% Maximum Degradation of IRAK4 and Ikaros observed at 3 mg/kg D1,2 dosing

In patient-derived xenograft models *in vivo*, KT-413 showed single-agent antitumor activity, including inducing tumor regressions in multiple models of MYD88-mutated DLBCL at well-tolerated doses (Figure 16).

Figure 16. KT-413 Shows Regressions in MYD88-mutant Patient-Derived Xenograft Models.



In summary, these preclinical data show that KT-413 is able to affect similar levels of IRAK4 and IMiD substrates degradation and antitumor activities in a dose-dependent manner *in vivo* using either PO or IV formulations. Together, given the potential for intermittent and discontinuous dosing as sufficient to drive deep and sustained regressions, we believe these data support the potential for KT-413 as a transformative therapy that synergistically combines the activity of both IRAK4 and IRAKIMiD substrate degradation to exploit complimentary pathway signaling.

Developing IRAK4-selective Degraders for Other Hematologic Malignancies and Solid Tumors

In addition to our IRAKIMiD program, we are also exploring the therapeutic potential of IRAK4-selective degradation without IMiD biology, in both liquid and solid tumors, as there are certain cancers where this approach may be effective either as a monotherapy or in a combination therapy. Potential indications could include MYD88-mutant Waldenstrom’s macroglobulinemia, subsets of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), and non-small cell lung cancer. This program is in an earlier stage of development.

STAT3 Degradar for Cancer and Autoimmune/Fibrotic Diseases

Summary

We are developing our selective STAT3 degraders for the treatment of hematological malignancies and solid tumors, as well as autoimmune diseases and fibrosis. STAT3 is a transcription factor activated through a variety of different cytokine and growth factor receptors via JAKs, as well as through oncogenic fusion proteins and mutations in STAT3 itself. We believe the diverse functions of STAT3 in tumor biology, evasion of immune surveillance by tumor cells, and inflammation and fibrosis provide opportunities to address a wide variety of high unmet need disease indications through the targeting of a single genetically and clinically validated pathway. While the JAK-STAT pathway has been partially addressed with several clinically successful JAK-targeting agents, we believe there are currently no drugs that specifically affect STAT3 broadly across all the relevant cell types. Small molecule STAT3 dimerization inhibitors targeting the SH2 domain have been in development, but significant challenges remain: first, homology of SH2 domains among all STAT family members impacts the ability to achieve specificity for STAT3, and second, inability to block dimerization independent transcriptional activities of STAT3. For these reasons, we believe that STAT3 degraders may provide a transformative solution to develop targeted and specific drugs to address multiple STAT3 dependent pathologies.

In February 2021, we nominated KT-333 as our STAT3 development candidate for liquid and solid tumor indications, and we have initiated IND-enabling activities. We expect to submit an IND to the FDA in the fourth quarter of 2021 and, if cleared, initiate a Phase 1 trial thereafter. KT-333 has demonstrated high potency and selectivity in both *in vitro* and *in vivo* preclinical models, including significant and sustained anti-tumor activity in several preclinical models of liquid and solid tumors.

Biology and Mechanism of Action of STAT3 Degradator

STAT3 (signal transducer and activator of transcription 3) is a transcription factor and a member of the STAT protein family. In response to cytokines and growth factors, STAT3 is phosphorylated by receptor-associated serine/threonine kinases, and phosphorylated STAT3, or p-STAT3, then forms dimers that translocate into the nucleus, bind to DNA, and regulate transcription of a wide variety of genes involved in oncogenesis, inflammation and fibrosis. STAT3 is frequently mutated and activated in numerous cancers, including clinically aggressive hematologic malignancies with high unmet medical need. Mechanistically, aberrant activation of STAT3 has been directly linked to the promotion of cancer cell survival, proliferation, and metastasis. In addition, STAT3 regulates the crosstalk between tumor, stroma, and immune cells to promote an immunosuppressive tumor microenvironment. STAT3 activation by IL-6 and TGF- β is also involved in the pathogenesis of autoimmunity and fibrosis. These various roles of STAT3 in disease pathogenesis make it an attractive target for drug development in cancer and autoimmune and fibrotic diseases.

Differentiation from JAK and IL-6 Inhibitors

Small molecule inhibitors against JAK family kinases, such as JAK1, JAK2, JAK3, and TYK2, have been approved for the treatment of autoimmune diseases such as RA, psoriatic arthritis, and ulcerative colitis and target the JAK2/STAT5 pathway. In oncology, JAK inhibitors have been approved for hematological malignancies with mutations leading to activation of the JAK2/STAT5 pathway, including primary myelofibrosis and polycythemia vera, and for acute graft versus host disease. JAK inhibitors block signaling of a number of cytokines and growth factors and reduce activation not only of STAT3 but also STAT1 and STAT5 in response to these stimuli. For modulating anti-tumor effects, this broad activity may have conflicting consequences. In particular, the inhibition of STAT1 activity dampens anti-tumor immune responses by cytolytic T cells and antigen presenting cells, thereby counteracting a productive immune response that could be achieved by inhibition of STAT3 alone. As a result, JAK inhibitors have not shown clinical activity in cancer beyond the myeloproliferative neoplasms. The broad activity of JAK inhibitors is also associated with class-specific adverse effects. By targeting STAT3 selectively, these immunosuppressive and safety liabilities associated with broader STAT1 and STAT5 inhibition through JAK inhibition may be avoided while also effectively addressing JAK-dependent and independent activation of STAT3.

Monoclonal antibodies directed against pro-inflammatory cytokines such as IL-6 or their receptors IL-6R have also been approved for select autoimmune diseases. However, autoimmune and fibrotic diseases and certain cancers are often regulated by multiple cytokines. As such, targeting STAT3 has the potential to be more effective since it is involved in signaling by not just IL-6, but also by TGF- β and cytokines such as IL-12, IL-2 and IL-15. Consequently, targeting STAT3 directly has the potential to block multiple signaling pathways that converge on STAT3 and reverse pathological processes that contribute to a tumor-permissive microenvironment.

Pre-IND Status and Next Steps

KT-333 is in IND-enabling activities and we expect to file an IND with the FDA in the fourth quarter of 2021 and, if cleared, initiate a Phase 1 trial thereafter. Our Phase 1 clinical trial in hematological malignancies and solid tumors is expected to include dose escalation and assess safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary clinical activity. We expect that our Phase 1b clinical trial using the optimal dose and schedule from Phase 1 will include multiple expansion cohorts intended to assess clinical activity across different STAT3-dependent hematologic malignancies and solid tumors. We believe early development data from our STAT3 degraders in oncology will help inform subsequent development in autoimmunity and fibrosis indications.

Development Opportunities

The multiple effects of a STAT3 degrader on oncogenesis, tumor cell resistance to tyrosine kinase inhibitors and chemotherapy, and evasion of immune surveillance provide multiple development opportunities in hematologic malignancies and solid tumors. Additionally, the role of STAT3 in chronic inflammation and fibrosis, as also observed in patients with germline STAT3 gain-of-function mutations, informs opportunities in autoimmune and fibrotic diseases.

Hematologic Malignancies

Oncogenic STAT3 mutations and/or STAT3 pathway activations are highly common in peripheral T-cell lymphoma, or PTCL, and cutaneous T-cell lymphoma, or CTCL, indications with an estimated US incidence of approximately 5,000 and 2,000 annual cases, respectively. STAT3 mutations and pathway activations along with responsiveness of PTCL subsets and CTCL to immune checkpoint inhibitors point to a dependency on STAT3 in these indications and therefore the opportunity to develop a STAT3 degrader as a monotherapy. The standard of care for first-line treatment of PTCL is the combination of brentuximab vedotin, a CD30-directed antibody-drug conjugate, and chemotherapy. The majority of PTCL patients, including ALK-ALCL, PTCL-Not Otherwise Specified, AITL and NK/T lymphoma subtypes, eventually progress and die of their disease. For patients with refractory/relapsed disease, current treatment options are limited and approved therapies pralatrexate and romidepsin have shown limited efficacy. High prevalence of STAT3 mutations (approximately 13-38%) and STAT3 pathway activation (up to 90%) is found in these refractory/relapsed PTCL subsets with high unmet need. Given the documented effect of STAT3 downregulation on levels of programmed death-ligand 1, or PD-L1, we expect our STAT3 degrader to have a dual effect in these patients. In CTCL patients with advanced stage disease and the highest levels of STAT3 activation, there are no curative therapies and no standard of care. Antibody-drug conjugates, HDAC inhibitors, and immune checkpoint inhibitors have some activity and are used upfront or in refractory/relapsed patients, but there remains a high unmet need for an effective therapeutic with both tumor-intrinsic as well as immunomodulatory antitumor effects.

STAT3 pathway activation is also present in virtually all patients with T- and NK-cell large granular lymphocytic leukemia, and up to 70% of patients have oncogenic STAT3 mutations. These findings are highly indicative of STAT3 dependency, which is further supported by the preliminary clinical activity of JAK inhibitors in these patients. STAT3 activation is also commonly observed in AML and in DLBCL even though STAT3 mutations are infrequent. PD-L1 overexpression in DLBCL has been linked to worse disease outcomes and responses to anti-PD-1/PD-L1 drugs have been reported in these patients. Given STAT3 has downstream impact on PD-1/PD-L1, we believe that a STAT3 degrader has the potential to achieve profound clinical effects both as a monotherapy and in combination with other active drugs.

Solid Tumors

Cancers that are responsive to anti-PD-1/PD-L1 immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs), including non-small cell lung cancer, or NSCLC, head and neck squamous cell carcinoma, or HNSCC, breast cancer and colorectal cancer, are compelling development opportunities due to the established role of STAT3 in solid tumor resistance to ICIs and TKIs. Specifically, STAT3 degraders have the potential to improve responses upfront in combination with these modalities or overcome acquired resistance as add-on therapy in second-line.

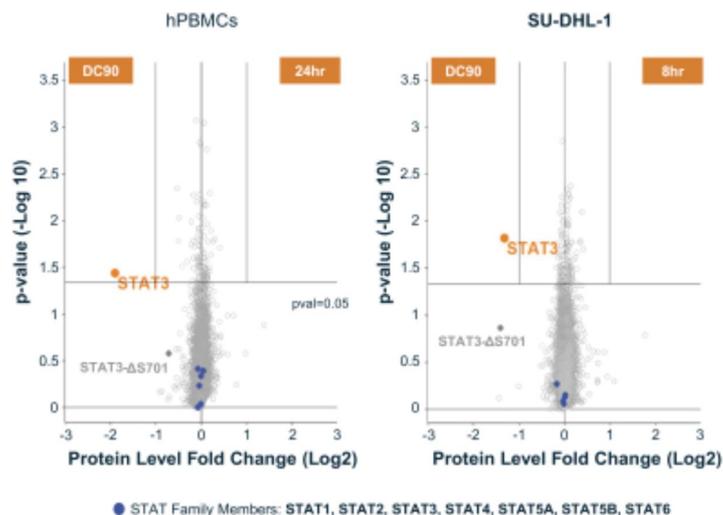
Autoimmune and Fibrotic Diseases

Patients with rare germline STAT3 gain-of-function mutations develop multiple autoimmune and fibrotic diseases, including systemic sclerosis, or SSc, AD, interstitial lung disease, enteropathies, and RA. We believe these manifestations, and their response to JAK inhibitors, provide support for STAT3 degrader development in immunology and inflammation. There are numerous publications that highlight the role of STAT3-mediated IL-6 and TGF- β signaling in the pathogenesis of SSc, idiopathic pulmonary fibrosis, or IPF, Crohn's disease, and multiple sclerosis. There remains a high unmet need for drugs that can target both the inflammation and fibrosis in SSc and IPF and halt or reverse disease progression. A STAT3 degrader has the potential for this dual effect and could therefore provide a transformative approach to treating both IPF as well as the various clinical manifestations of SSc.

Hematologic Malignancies—In Vitro Data

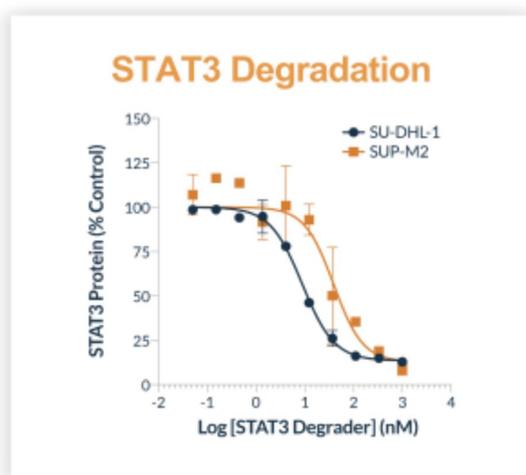
We performed deep mass spectrometry-based proteomics to assess the specificity of a STAT3 degrader tool compound. In the example below, hPBMC and tumor cells (SU-DHL-1) were treated with the STAT3 degrader tool compound to assess its ability to affect protein levels on a proteome scale. As shown below, measurement of over 10,000 proteins showed that STAT3 is the only protein degraded by the tool compound with statistical significance, demonstrating its highly selective degradation profile (Figure 17).

Figure 17. Proteomic Analysis of STAT3 Degradation Selectivity in hPBMCS and SU-DHL-1 with a STAT3 Degradation Tool Compound.



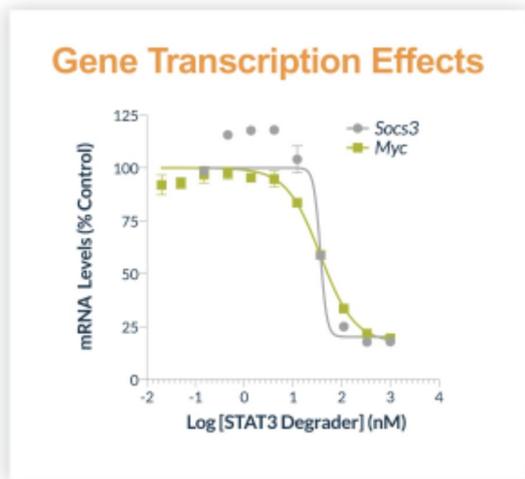
To assess the *in vitro* degradation potency of the STAT3 degrader tool compound, we measured STAT3 protein levels in two STAT3-dependent ALK+ ALCL cell lines SU-DHL-1 and SUP-M2 after 24 hours of drug exposure. As shown in Figure 18, the tool compound decreased the levels of STAT3 by greater than 95% with a DC50 of 15 nM and 86 nM, respectively.

Figure 18. Cellular Degradation of STAT3 in SU-DHL-1 and SUP-M2 Cell Lines Upon Treatment with a STAT3 Degradation Tool Compound.



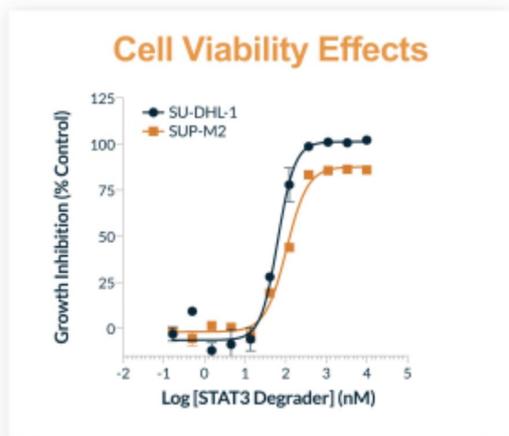
As STAT3 plays a role in regulating gene expression, we measured the expression of downstream target genes in SU-DHL-1 cells treated with a STAT3 degrader tool compound. As shown in Figure 19, treatment with the tool compound for 24 hours also led to significant downregulation of STAT3 target genes, such as SOCS3 and MYC, with IC50 of 36 and 37 nM, respectively.

Figure 19. Effect of a STAT3 Degradation Tool Compound on STAT3-Dependent Gene Expression in SU-DHL-1 Cells.



In order to assess the impact of STAT3 degradation on viability of lymphoma cells, we treated SU-DHL-1 and SUP-M2 cells with a STAT3 degrader tool compound for 96 hours and evaluated cell growth inhibition. As shown in Figure 20, the tool compound inhibited the growth of both SU-DHL-1 and SUP-M2 cells with IC50 values of 64 and 105 nM, respectively. Additionally, a separate *in vitro* experiment revealed that 48 hours compound treatment with greater than 90% degradation led to the complete inhibition of cell growth.

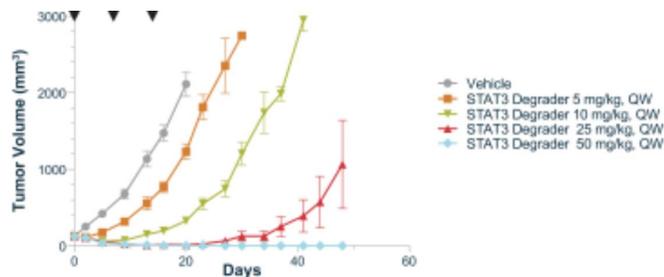
Figure 20. Growth Inhibition of SU-DHL-1 and SUP-M2 Cell Lines Upon Treatment with a STAT3 Degradation Tool Compound.



Hematologic Malignancies—*In Vivo* Data

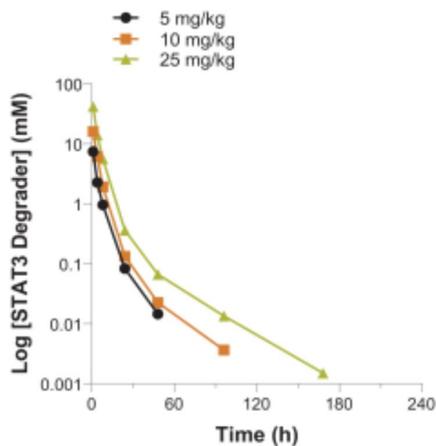
To evaluate the *in vivo* activity of a STAT3 degrader tool compound, we used the ALK+ ALCL SU-DHL-1 xenograft mouse model. Mice were administered the tool compound intravenously once a week and monitored for tumor volume over time. As shown in Figure 21, the tool compound showed tumor responses with complete regressions and durable responses when dosed at 50mg/kg dose.

Figure 21. Regression in SU-DHL-1 Xenograft Tumors Upon Weekly Dosing of a STAT3 Degradator Tool Compound.



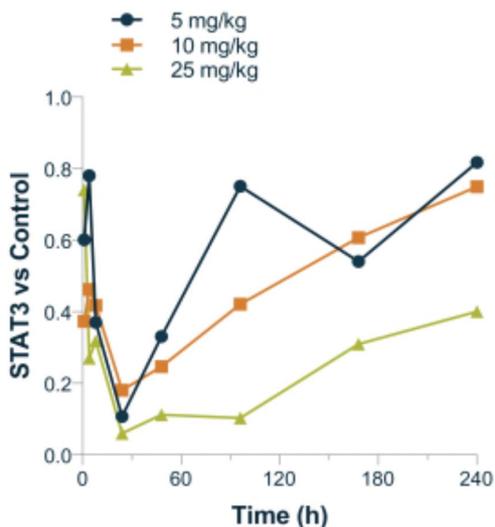
We characterized the degradation profile of STAT3 in a SU-DHL-1 mouse xenograft model following single intravenous administration. A STAT3 degrader tool compound exhibited a dose-dependent increase in plasma across the dose range of 5 to 25 mg/kg (Figure 22).

Figure 22. Dose-Dependent Plasma Exposure in SU-DHL-1 Xenograft Mice Upon Single IV Dose of a STAT3 Degradator Tool Compound.



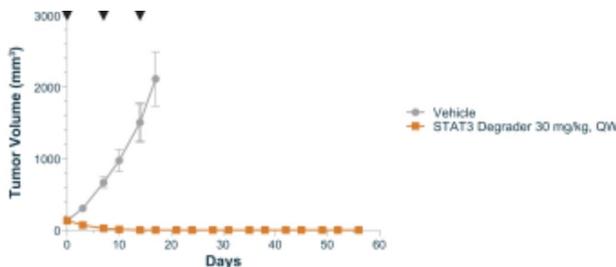
We assessed STAT3 degradation in tumors with a STAT3 degrader tool compound as a measure of pharmacodynamic effect and showed a dose-dependent reduction with maximal degradation of greater than 90% after 24 hours of a single intravenous administration. At 25 mg/kg, STAT3 levels in tumor were still below 50% of baseline ten days post-dose (Figure 23). The data demonstrated that tumor response was dependent on both the level and duration of STAT3 knockdown.

Figure 23. Dose-Dependent Reduction of STAT3 in SU-DHL-1 Xenograft Mice Upon Single IV Dose of a STAT3 Degradation Tool Compound.



To confirm the anti-tumor activity of a STAT3 degrader tool compound in additional STAT3-driven ALK+ ALCL models, we evaluated the effects of the degrader in the SUP-M2 xenograft model. Mice were dosed with 30mg/kg of our STAT3 degrader intravenously once a week for 3 weeks and monitored for tumor volume over time. As shown in Figure 24, the tool compound induced complete regression of SUP-M2 tumors that was durable for multiple weeks after the last dose.

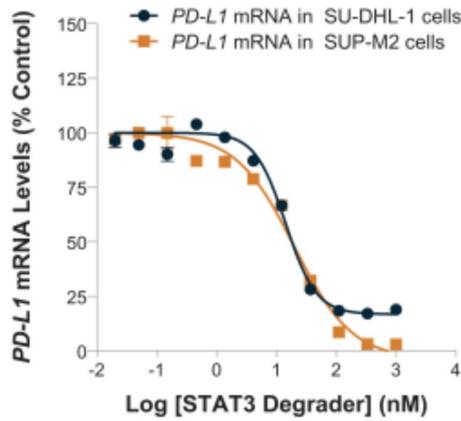
Figure 24. Regression in SUP-M2 Xenograft Tumors Upon Weekly Dosing of a STAT3 Degradation Tool Compound.



Immuno-Oncology Mechanism—In Vitro Data

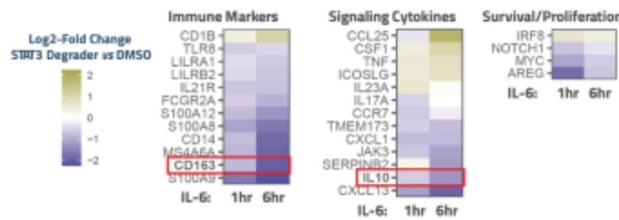
STAT3 degradation with a STAT3 degrader tool compound has demonstrated tumor-intrinsic and tumor-extrinsic effects that may contribute towards restoring an immune-permissive tumor microenvironment. A mechanism by which tumor cells evade immune surveillance is through increased expression of PD-L1 that interacts with PD-1, an immune checkpoint protein expressed on activated T cells that leads to the inhibition of T cell function. As shown in Figure 25, treatment of SU-DHL-1 or SUP-M2 ALC cells with the tool compound for 24 hours reduced transcription of PD-L1 mRNA indicating that STAT3 degradation may reverse a key tumor-intrinsic mechanism for immune suppression.

Figure 25. Reduced Transcription of PD-L1 mRNA Upon 24 Hour Dose of a STAT3 Degradator Tool Compound.



To assess the effect of STAT3 on the gene expression of immune-suppressive cytokines and immune-regulatory factors, we stimulated hPBMC with IL-6 in the presence or absence of a STAT3 degrader tool compound. The results below show that the tool compound blocked IL-6-induced increases in the expression of genes involved with immune suppression, including immune markers (e.g., CD163), and signaling cytokines (e.g., IL-10) (Figure 26). Collectively, these data show that degradation of STAT3 in tumor and immune cells reverses expression of genes that contribute to immune suppression and highlights the potential of STAT3 degraders as immunotherapies.

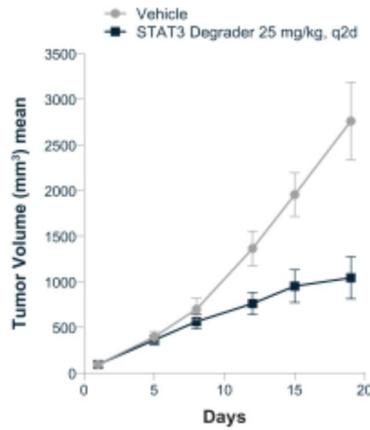
Figure 26. Reduced Gene Expression of Immune-suppressive Cytokines and Immune-regulatory Factors with a STAT3 Degradator Tool Compound.



Immuno-Oncology Mechanism—In Vivo Data

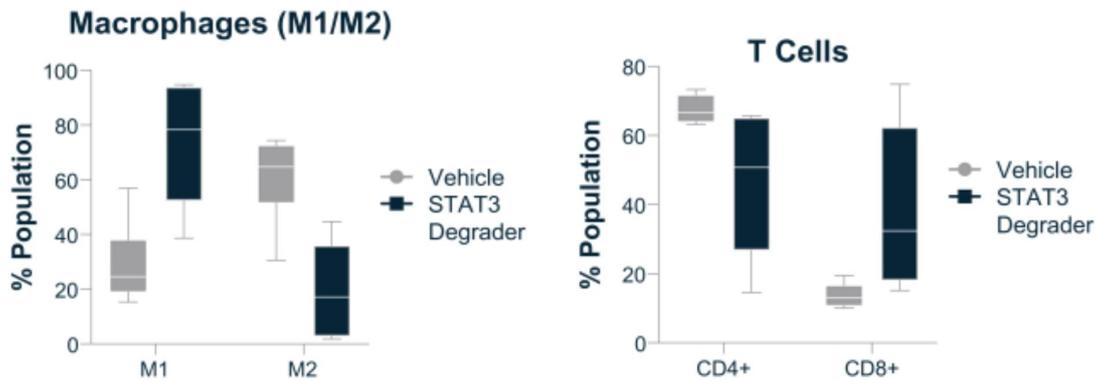
To assess the *in vivo* effect of a STAT3 degrader tool compound on modulating tumor immunity, we conducted a study using CT-26 syngeneic colorectal cancer tumors known to be refractory to approved immunotherapies like PD-1 and PD-L1. We observed that the tool compound significantly reduced tumor growth when administrated every two days at 25 mg/kg (Figure 27).

Figure 27. Modulating Tumor Immunity with a STAT3 Degradation Tool Compound.



We performed flow cytometry analysis of tumors from the same study to assess whether the anti-tumor effect was related to changes in the abundance of infiltrating immune cells in the tumor. The results showed a decreased number of immuno-suppressive M2 macrophages and CD4+ T cells relative to the vehicle and an increased number of anti-tumor M1 macrophages and cytolytic effector CD8+ T cells relative to the vehicle (Figure 28). The data demonstrate a synergistic modulation of immune cells within the tumor microenvironment to favor an anti-tumor response.

Figure 28. Synergistic Modulation of Immune Cells within Tumor Microenvironment.



We believe these results demonstrate the favorable immunomodulatory effects of STAT3 downregulation in both tumor cells and the tumor microenvironment associated with antitumor activity, underscoring the therapeutic potential of STAT3 degraders in oncology based on both tumor cell intrinsic and extrinsic biology.

Cell Intrinsic Mechanism in Solid Tumors

Through its regulation of cell survival genes, STAT3 is activated across a wide range of cancer cells in response to TKIs and chemotherapies. Prolonged activation of STAT3 is associated with selection for tumor cells that are tolerant to the therapy, eventually leading to resistance and disease progression. A STAT3 degrader could therefore be used in combination with TKIs and/or chemotherapy, either upfront as a way to deepen and maintain response to first-line treatment, or as an add-on in second-line therapy to overcome acquired resistance to frontline therapy.

In EGFR mutant non-small cell lung cancer, or NSCLC, treatment with an EGFR kinase inhibitor such as erlotinib leads to upregulation of p-STAT3 indicating STAT3 activation. This is not observed in EGFR wild type NSCLC, pointing to STAT3 as a potential resistance mechanism. In fact, when we treated the EGFR mutant NSCLC cell line H1650 with erlotinib, we observed an upregulation of p-STAT3 which was reversed in the presence of a STAT3 degrader tool compound. We are expanding these efforts to *in vivo* studies to complete our preclinical research to validate STAT3 degradation as a new mechanism for first line EGFR mutant therapy in NSCLC.

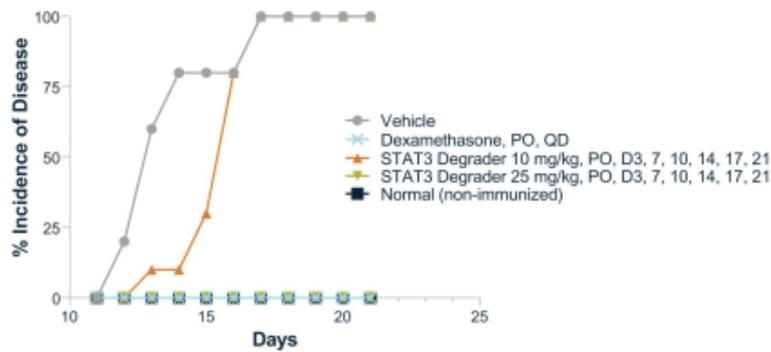
Figure 29. A STAT3 degrader tool compound reverses pSTAT3 upregulation when administered in combination with an EGFR inhibitor.



Autoimmunity

We are also exploring the effects of STAT3 in several immunology-inflammation *in vitro* and *in vivo* models. In a preclinical model of experimental autoimmune encephalomyelitis, a STAT3 degrader tool compound was able to completely prevent the onset of the disease in mice and was equivalent to steroid treatment with dexamethasone (Figure 30). These data, together with *in vitro* mechanisms of action studies that we are conducting, highlight the potential of STAT3 degradation for the treatment of immunology-inflammation disease.

Figure 30. A STAT3 Degradator Tool Compound is Highly Active in Experimental Autoimmune Encephalomyelitis Model.

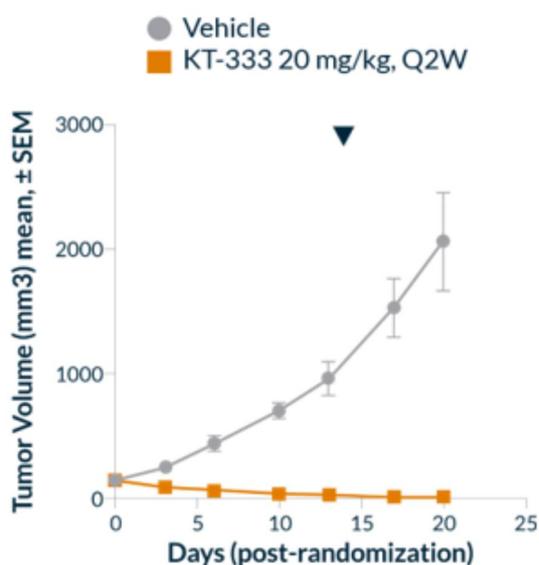


In February 2021, we nominated KT-333 as our STAT3 development candidate for liquid and solid tumor indications, and we have initiated IND-enabling activities. We expect to submit an IND to the FDA in the fourth quarter of 2021 and, if cleared, initiate a Phase 1 trial thereafter. KT-333 has demonstrated high potency and selectivity in both *in vitro* and *in vivo* preclinical models, including significant and sustained anti-tumor activity including significant and sustained anti-tumor activity in several preclinical models of liquid and solid tumors.

Figure 31. KT-333 STAT3 Degradation Development Candidate is Highly Active *In Vitro*.

	KT-333 <i>in vitro</i> Potency
STAT3 DC ₅₀ in A549 (nM)	4.7
STAT3 DC ₅₀ (SU-DHL-1) (nM)	3
SU-DHL-1 viability IC ₅₀ (nM)	40
SUP-M2 viability IC ₅₀ (nM)	8

Figure 32. KT-333 STAT3 Degradation Development Candidate Demonstrates *in vivo* Tumor Growth Regression.



Other Programs

Our focus on key undrugged or inadequately drugged nodes within therapeutically validated pathways combined with the target and disease agnostic features of our Pegasus™ platform gives us opportunity to develop new therapies across various therapeutic areas. We are taking advantage of our proprietary E3 Ligase Whole-Body Atlas on the differential expression profile of E3 ligases to pursue targets that can benefit from potentially tissue-restricted degradation. Our early pipeline includes programs in genetically defined oncology and immunology indications. Through our Vertex collaboration, we are engaged in the discovery of additional targets that are able to fully leverage our aforementioned capabilities and expand our impact across several diseases outside of oncology and immunology.

Collaborations

Collaboration Agreement with GlaxoSmithKline Intellectual Property Development Limited

On October 3, 2017, we entered into a collaboration agreement with GlaxoSmithKline Intellectual Property Development Limited, or GSK, to jointly identify, research and conduct preclinical development of collaboration compounds against specified collaboration targets to identify drug candidates. We refer to this agreement as the GSK Agreement.

Under the GSK Agreement, GSK is using its DNA-encoded libraries, which can be used to scan trillions of compounds tagged with DNA bar codes that can be sequenced to reveal the structure of any hits, to screen a limited number of drug discovery targets of interest. The GSK Agreement also provides that the parties will collaborate to discover novel ligase binders. The GSK Agreement supports ongoing collaboration between the parties, with each party having a right to use certain insights gained in the collaboration for its own programs. The GSK Agreement also provides a mechanism for GSK to negotiate to license certain collaboration programs.

GSK has granted us a royalty-bearing, exclusive, non-transferrable, worldwide, sublicenseable right and license to research, develop and commercialize certain compounds.

As partial consideration for this agreement, we issued GSK 886,305 Series A preferred units of Kymera Therapeutics, LLC. In addition, low single-digit royalties would become payable by us to GSK on worldwide net sales in a given calendar year if a product comprising certain licensed compounds were to be commercialized. Royalties would be payable on a product-by-product and country-by-country basis for a period commencing upon the first commercial sale of any such product and continuing for ten (10) years thereafter.

Unless earlier terminated, the GSK Agreement will continue on a product-by-product and country-by-country basis until there are no more royalty payments owed to GSK on any product under the agreement. Either party may terminate the GSK Agreement upon an uncured material breach, or upon the bankruptcy, insolvency, dissolution or winding up of the other party. The GSK Agreement may also be terminated by either party for convenience upon sixty (60) days' prior written notice to the other party.

Master Collaboration Agreement with Vertex Pharmaceuticals Incorporated

On May 9, 2019, we entered into a collaboration agreement with Vertex, focused on the research and development of our small molecule targeted protein degraders against multiple targets in disease areas outside our core strategic focus. The collaboration leverages our expertise in targeted protein degradation and our PegasusTM platform as well as Vertex's scientific, clinical, and regulatory capabilities to accelerate the development of medicines for people with serious diseases. We refer to this agreement as the Vertex Agreement.

Under the terms of the Vertex Agreement, we conduct research activities in multiple targets pursuant to an agreed-upon research plan. Upon designation of a clinical development candidate, Vertex has the option to exclusively license molecules against the designated target. We are eligible to receive an aggregate of up to \$170 million in potential payments per licensing product based upon the successful achievement of specified research, development, regulatory and commercial milestones, as well as option exercise payments, for up to six (6) programs optioned by Vertex for licensing as part of the collaboration. No milestones have been achieved to date under the Vertex Agreement.

In addition, Vertex will pay low single-digit royalties on future net sales on any products that may result from the commercialization of the licensed molecules. Vertex's royalty obligations are on a product-by-product and country-by-country basis and are subject to certain reductions, including (i) in the event that the exploitation of a product is not covered by a valid claim with the licensed patent rights and (ii) in the event of third parties achieving specifically negotiated levels of competitive market share. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the later of (a) the expiration of the last patent which covers a product in such country, (b) the expiration of any exclusivity granted by a regulatory authority and (c) 10 years following the first commercial sale of a product in such country. No additional payments have been made by Vertex under the Vertex Agreement to date.

As initial consideration for the collaboration, Vertex paid us \$70 million upfront including an equity investment in us through the purchase of 3,059,695 shares of our Series B-1 preferred stock. In connection with its equity investment, Vertex holds certain rights to invest, in its sole discretion, in future private placements or public securities offerings by Kymera, on a pro rata basis and subject to certain conditions.

Under the Vertex Agreement, the parties established a joint advisory committee, or JAC. The JAC will, among other responsibilities, review and oversee, certain strategic activities performed under the Vertex Agreement, including reviewing the research plan and budget for the research activities and reviewing the research activities performed by each party.

The initial research term of the collaboration is four years, extendable for an additional one-year period upon mutual agreement by the parties and payment by Vertex of certain per-target fees.

The Vertex Agreement may be terminated by Vertex either in its entirety or on a target-by-target basis, upon prior written notice to Kymera. Either party may terminate the collaboration agreement upon the other party's material breach, subject to specified notice and cure provisions, or upon the bankruptcy, insolvency, dissolution or winding up of the other party. Kymera also has the right to terminate the agreement with respect to a certain target upon 30 days' prior written notice in the event that Vertex ceases all research, development and commercialization activities related to such target for a certain period of time, provided that the cessation is not the result of events outside of Vertex's control.

Collaboration Agreement with Genzyme Corporation

On July 7, 2020, we entered into a collaboration agreement, or the Sanofi Agreement, with Genzyme Corporation, a subsidiary of Sanofi, to co-develop drug candidates directed to two biological targets. The Sanofi Agreement became effective during the third quarter of 2020.

Under the Sanofi Agreement, Kymera grants to Sanofi a worldwide exclusive license to develop, manufacture and commercialize certain lead compounds generated during the collaboration directed against IRAK4 and one additional undisclosed target in an undisclosed field of use. Such license is exercisable on a collaboration target-by-collaboration target basis only after a specified milestone. For compounds directed against IRAK4, the field of use includes diagnosis, treatment, cure, mitigation or prevention of any diseases, disorders or conditions, excluding oncology and immuno-oncology.

Pursuant to the Sanofi Agreement, with respect to both targets we are responsible for discovery and preclinical research and conducting a phase 1 clinical trial for at least one degrader directed against IRAK4 plus up to three back up degraders, the costs of which will be borne by us, except in certain circumstances. With respect to both targets, Sanofi is responsible for development, manufacturing, and commercialization of product candidates after a specified development milestone occurs with respect to each collaboration candidate.

In addition, pursuant to the Sanofi Agreement, Sanofi will grant to us an exclusive option, or Opt-In Right, exercisable, at our sole discretion, on a collaboration target-by-collaboration target basis that will include the right to (i) fund 50% of the United States development costs for collaboration products directed against such target in the applicable field of use and (ii) share equally in the net profits and net losses of commercializing collaboration products directed against such target in the applicable field of use in the United States. In addition, if we exercise our Opt-In Right, Sanofi will grant to us an exclusive option, applicable to each collaboration target, which upon exercise will allow us to conduct certain co-promotion activities in the field in the United States.

In consideration for the exclusive licenses granted to Sanofi under the Sanofi Agreement, Sanofi paid to us an upfront payment of \$150 million. In addition to the upfront payment, we will also be eligible to receive certain development milestone payments of up to \$1.48 billion in the aggregate, of which more than \$1.0 billion relates to the IRAK4 program, upon the achievement of certain developmental or regulatory events. We will also be eligible to receive certain commercial milestone payments up to \$700 million in the aggregate, of which \$400 million relates to the IRAK4 program, which are payable upon the achievement of certain net sales thresholds. We will further be eligible to receive tiered royalties for each program on net sales ranging from the high single digits to high teens, subject to low-single digits upward adjustments in certain circumstances.

The Sanofi Agreement, unless earlier terminated, will expire on a product-by-product basis on the date of expiration of all payment obligations under the Sanofi Agreement with respect to such product. We or Sanofi may terminate the agreement upon the other party's material breach or insolvency or for certain patent challenges. In addition, Sanofi may terminate the agreement for convenience or for a material safety event upon advance prior written notice, and we may terminate the agreement with respect to any collaboration candidate if, following Sanofi's assumption of responsibility for the development, commercialization or manufacturing of collaboration candidates with respect to a particular target, Sanofi ceases to exploit any collaboration candidates directed to such target for a specified period.

Manufacturing / Supply Chain

We do not own or operate manufacturing facilities for the production of our drug candidates and currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We currently engage with third-party contract manufacturing organizations, or CMOs, for the manufacture of our drug candidates for preclinical studies, and we intend to continue to do so in the future. We rely on and expect to continue to rely on third-party manufacturers for the production of both drug substance and finished drug product. We have engaged third-party manufacturers to supply the drug substances for our drug candidates and a third-party manufacturer to develop and manufacture finished drug product for KT-474 that we are using in our Phase 1 clinical trial. We currently obtain our supplies from these manufacturers on a purchase order basis and do not have long-term supply arrangements in place. Should any of these manufacturers become unavailable to us for any reason, we believe that there are a number of potential replacements, although we may incur some delay in identifying and qualifying such replacements.

All of our drug candidates are organic compounds of low molecular weight, generally called small molecules, but which are larger than traditional small molecule therapeutics. We have selected these compounds not only on the basis of their potential efficacy and safety, but also because we anticipate an ease of synthesis and cost of goods. We have produced drug substances and drug product for use in our KT-474 Phase 1 clinical trial, and continue to refine our production processes. The drug substance and drug product processes are amenable to scale-up and do not require unusual equipment in the manufacturing process. To adequately meet our needs for late-stage clinical and commercial manufacturing, our suppliers will need to scale their production, or we will need to secure alternate suppliers.

Competition

The biotechnology industry is extremely competitive in the race to develop new products. While we believe we have significant competitive advantages with our years of expertise in targeted protein degradation, clinical development expertise, and intellectual property position, we currently face and will continue to face competition for our development programs from companies that use targeted protein degradation or targeted protein degradation development platforms, and from companies focused on more traditional therapeutic modalities such as small molecules and antibodies. The competition is likely to come from multiple sources, including larger pharmaceutical companies, biotechnology companies, and academia.

Competitors in our efforts to develop small molecule protein degraders therapies for patients, include, but are not limited to, Arvinas, Inc., which we believe is in clinical development, and C4 Therapeutics, Inc., Nurix Therapeutics, Inc., Foghorn Therapeutics, Inc., and Vividion Therapeutics, Inc., each of which we believe is in preclinical development. Further, several large pharmaceutical companies have disclosed preclinical investments in this field. Our competitors will also include companies that are or will be developing other targeted protein degradation methods as well as small molecule, antibody, or gene therapies for the same indications that we are targeting. In addition to the competitors we face in developing small molecule protein degraders, we will also face competition in the indications we expect to pursue with our IRAK4, IRAKIMiD and STAT3 programs. Many of these indications already have approved standards of care which may include more traditional therapeutic modalities. In order to compete effectively with these existing therapies, we will need to demonstrate that our protein degrader therapies are favorable to existing therapeutics.

Intellectual Property

Our success depends in part on our ability to secure intellectual property protection for our product candidates and future products, as well as our platform protein degradation technologies and any other relevant inventions and improvements that are considered commercially important to our business. Our success also depends on our ability to defend and enforce our intellectual property rights, preserve the confidentiality of our proprietary information, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties.

As with other biotechnology and pharmaceutical companies, our ability to secure and maintain intellectual property protection for our product candidates, future products, and other proprietary technologies will depend on our success in obtaining effective patent coverage and enforcing those patents if granted. However, we cannot guarantee that our pending patent applications, and any patent applications that we may in the future file, will result in the issuance of patents, or that any issued patents we may obtain will provide sufficient proprietary protection from competitors. Any issued patents that we obtain may be challenged, invalidated, or circumvented by third parties.

In addition to patents, we also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary technology, in part, through confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and potential collaborators.

Patent Portfolio

Our intellectual property includes a portfolio of wholly owned patent families covering our platform E3 ligase ligand technology and our novel bifunctional degrader product candidates, including claims to compositions of matter, pharmaceutical compositions, methods of use, methods of treatment, and other related methods. Our intellectual property portfolio is in its very early stages, and, as of February 28, 2021, included one granted U.S. patent, 52 U.S. patent applications, and 53 foreign patent applications. Our patent portfolio is generally organized into two categories: (1) platform E3 ligase ligand patent families and (2) protein degrader patent families, including various target-specific degrader patent families.

Platform E3 Ligase Ligand Patent Families

Our platform E3 ligase ligand patent families are wholly owned and include four patent families directed to novel ligands for the cereblon E3 ubiquitin ligase, as well as methods of treatment and other related methods. As of February 28, 2021, our platform E3 ligase ligand patent families included three U.S. patent applications and four foreign patent applications, including one international patent application and three patent applications in Europe. Any U.S. or foreign patents resulting from these applications, if granted and all appropriate maintenance fees paid, are expected to expire between 2038 and 2040, absent any patent term adjustments or extensions.

Protein Degrader Patent Families

Our protein degrader patent families are wholly owned and are directed to novel bifunctional degrader compounds that are useful in affecting ubiquitination of a target protein, as well as methods of treatment and other related methods. As of February 28, 2021, our protein degrader patent families included four U.S. patent applications and 12 foreign patent applications, including one international patent application and 11 patent applications filed in Europe, Australia, Canada, Hong Kong, Israel, Japan, Mexico, New Zealand, and the Russian Federation. Any U.S. or foreign patents resulting from these applications, if granted and all appropriate maintenance fees paid, are expected to expire between 2038 and 2041, absent any patent term adjustments or extensions.

Target-Specific Degrader Patent Families

Our target-specific degrader patent families are wholly owned and focus protection around degrader compounds that are designed to target specific proteins for degradation, as well as methods of treatment and other related methods. Such targets include, for example, IRAK (interleukin-1 receptor-associated kinases) and STAT (signal transducers and activators of transcription). As of February 28, 2021, our target-specific degrader patent families included one granted U.S. patent, 45 U.S. patent applications and 37 foreign patent applications, including 17 international patent applications and 20 patent applications filed in Europe, Australia, Brazil, Canada, Eurasia, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, Taiwan. Any U.S. or foreign patents resulting from our target-specific degrader patent families, if granted and all appropriate maintenance fees paid, are expected to expire between 2038 and 2041, absent any patent term adjustments or extensions.

IRAK-Specific Patent Families

Our IRAK-specific patent families are wholly owned and include patent families covering degrader compounds that are designed to specifically target IRAK for degradation and patent families covering novel IRAK ligands. As of February 28, 2021, our IRAK-specific patent families included one granted U.S. patent, 28 U.S. patent applications, nine international patent applications, and 16 patent applications filed in Europe, Australia, Argentina, Brazil, Canada, Eurasia, Gulf Cooperation Council, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, and Taiwan. Any U.S. or foreign patents resulting from our IRAK-specific patent families, if granted and all appropriate maintenance fees paid, are expected to expire between 2038 and 2042, absent any patent term adjustments or extensions.

With respect to the KT-474 product candidate, we own six pending U.S. provisional patent applications, one allowed U.S. non-provisional patent application and one pending international patent application, each with claims directed to compositions of matter covering KT-474 and/or methods of making or using KT-474. Any U.S. or foreign patents resulting from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire between 2039 and 2041, absent any patent term adjustments or extensions.

STAT-Specific Patent Families

Our STAT-specific patent families are wholly owned and focus on degrader compounds that are designed to specifically target signal transducers and activators of transcription (STAT) for degradation. As of February 28, 2021, our STAT-specific patent families included six U.S. patent applications, one international patent application, and one patent application in Taiwan. Any U.S. or foreign patents resulting from our STAT-specific patent families, if granted and all appropriate maintenance fees paid, are expected to expire between 2040 and 2041, absent any patent term adjustments or extensions.

Other Target-Specific Patent Families

As of February 28, 2021, we own 11 U.S. patent applications and 10 foreign patent applications, including 7 international patent applications and 3 patent applications filed in Argentina, Gulf Cooperation Council, and Taiwan, which focus on degrader compounds designed to specifically target other proteins. Any U.S. or foreign patents resulting from these patent families, if granted and all appropriate maintenance fees paid, are expected to expire between 2040 and 2042, absent any patent term adjustments or extensions.

The term of individual patents may vary based on the countries in which they are obtained. Generally, patents issued from applications filed in the United States are effective for 20 years from the earliest effective non-provisional filing date. In certain cases, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent, though the total patent term, including any extension, must not exceed 14 years following FDA approval. A patent can only be extended once, such that, if a single patent is applicable to multiple products, it can only be extended based on one product.

The duration of patents outside of the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective national filing date.

Similar patent term extension provisions are available in Europe and other foreign jurisdictions to extend the term of a patent covering an approved drug. When possible, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

Trademarks

We intend to file applications for trademark registrations in connection with our product candidates and other technologies in various jurisdictions, including the United States. We have applied to register both the KYMERA mark and the KYMERA THERAPEUTICS mark in the United States, Europe, and Canada. We also filed applications in the same jurisdictions for the mark IRAKIMiD, for pharmaceutical and medical preparations and therapeutics, as well as diagnostic reagents, for the treatment of oncology, autoimmune, immune-oncology and other related diseases. In addition, we filed applications in the United States for E3 HUMAN ATLAS and E3 LIGASE WHOLE BODY ATLAS in connection with pharmaceutical research and development and drug development and discovery services.

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs. We, along with our vendors, contract research organizations and contract manufacturers, will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our product candidates. The process of obtaining regulatory approvals of drugs and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

In the U.S., the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, as amended, its implementing regulations and other laws. If we fail to comply with applicable FDA or other requirements at any time with respect to product development, clinical testing, approval or any other legal requirements relating to product manufacture, processing, handling, storage, quality control, safety, marketing, advertising, promotion, packaging, labeling, export, import, distribution, or sale, we may become subject to administrative or judicial sanctions or other legal consequences. These sanctions or consequences could include, among other things, the FDA's refusal to approve pending applications, issuance of clinical holds for ongoing studies, suspension or revocation of approved applications, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before our product candidates are approved as drugs for therapeutic indications and may be marketed in the U.S. generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements;
- completion of the manufacture, under current Good Manufacturing Practices, or cGMP, conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- submission to the FDA of an IND application, which must become effective before clinical trials may begin;
- approval by an institutional review board, or IRB, or independent ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of a NDA;
- a determination by the FDA within 60 days of its receipt of an NDA, to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites that generated the data in support of the NDA;
- payment of user fees for FDA review of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the U.S.

Preclinical Studies and Clinical Trials for Drugs

Before testing any drug in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as *in vitro* and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety/toxicology studies. The results of the preclinical studies, together with manufacturing information and analytical data must be submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before clinical trials may begin. Some long-term preclinical testing may continue after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research patients will be exposed to unreasonable health risks, and imposes a full or partial clinical hold. FDA must notify the sponsor of the grounds for the hold and any identified deficiencies must be resolved before the clinical trial can begin. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research patients provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable related to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. The FDA, the IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. Information about applicable clinical trials, including clinical trial results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, FDA will nevertheless accept the results of the study in support of an NDA if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials to evaluate therapeutic indications to support NDAs for marketing approval are typically conducted in three sequential phases, which may overlap.

- *Phase 1*—Phase 1 clinical trials involve initial introduction of the investigational product into healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, excretion the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- *Phase 2*—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the drug’s potential efficacy, to determine the optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.
- *Phase 3*—Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling.

In August 2018, the FDA released a draft guidance entitled “Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics,” which outlines how drug developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology drug development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to drug development and reduce development costs and time.

Post-approval trials, sometimes referred to as Phase 4 clinical trials or post-marketing studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor’s initial receipt of the information.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the drug product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Marketing Approval for Drugs

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. An NDA is a request for approval to market a new drug for one or more specified indications and must contain proof of the drug's safety and efficacy for the requested indications. The marketing application is required to include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be marketed in the U.S.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective for the indications sought and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. Under the goals and polices agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA and respond to the applicant, and six months from the filing date of a new molecular entity NDA for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy, or REMS, program if it believes that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh its risks. The REMS program could include use of risk evaluation and mitigation strategies like medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk-minimization tools.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act of 1983, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects more than 200,000 individuals in the U.S., there is no reasonable expectation that the cost of developing and making the product available in the U.S. for the disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan products are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of application fees.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Further, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs for Drugs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients earlier than under standard FDA development and review procedures.

A new drug is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as Priority Review, discussed below.

In addition, a new drug may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review designation and Accelerated Approval. A product is eligible for Priority Review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, the FDA must review an application in six months compared to ten months for a standard review.

Additionally, products are eligible for Accelerated Approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments.

Accelerated Approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. The FDA may withdraw approval of a drug or indication approved under Accelerated Approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, unless otherwise informed by the FDA, the FDA currently requires, as a condition for Accelerated Approval, that all advertising and promotional materials that are intended for dissemination or publication within 120 days following marketing approval be submitted to the agency for review during the pre-approval review period, and that after 120 days following marketing approval, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval but may expedite the development or review process.

Pediatric Information and Pediatric Exclusivity

Under the Pediatric Research Equity Act, or PREA, as amended, certain NDAs and certain supplements to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The FD&C Act requires that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 trial. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

A drug can also obtain pediatric market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial or of multiple pediatric trials in accordance with an FDA-issued "Written Request" for such trials.

U.S. Post-Approval Requirements for Drugs

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences with the product, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers and individuals working on behalf of manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-market testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and their subcontractors involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our contract manufacturers. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. There is also a continuing, annual prescription drug product program user fee.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or withdrawal of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; or mandated modification of promotional materials and labeling and issuance of corrective information.

Regulation of Companion Diagnostics

Companion diagnostics identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics are regulated as medical devices by the FDA. In the U.S., the FD&C Act, and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification, or 510(k), and approval of a premarket approval application, or PMA.

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a preamendment device that was in commercial distribution before May 28, 1976, or a predicate device, for which the FDA has not yet called for the submission of a PMA. In making a determination that the device is substantially equivalent to a predicate device, the FDA compares the proposed device to the predicate device and assesses whether the subject device is comparable to the predicate device with respect to intended use, technology, design and other features which could affect safety and effectiveness. If the FDA determines that the subject device is substantially equivalent to the predicate device, the subject device may be cleared for marketing. The 510(k) premarket notification pathway generally takes from three to twelve months from the date the application is completed, but can take significantly longer.

A PMA must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. The FDA's review of an initial PMA is required by statute to take between six months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny the approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

On July 31, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the premarket application for the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding in vitro companion diagnostic.

Once cleared or approved, the companion diagnostic device must adhere to post-marketing requirements including the requirements of the FDA's QSR, adverse event reporting, recalls and corrections along with product marketing requirements and limitations. Like drug makers, companion diagnostic makers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and our facilities for compliance with its authorities.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities of product candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the U.S. in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

Other healthcare laws

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

- The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid; a person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

- The federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using, or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs.
- The federal civil monetary penalties laws impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary, if the person knows or should know it is likely to influence the beneficiary’s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies.
- The Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, impose, among other things, specified requirements on covered entities and their business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions.
- The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program, for certain payments and “transfers of value” provided to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. In addition, many states also require reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made in the previous year to certain non-physician providers such as physician assistants and nurse practitioners.
- Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.
- Analogous state and foreign laws and regulations may be broader in scope than the provisions described above and may apply regardless of payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and relevant federal government compliance guidance; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers; restrict marketing practices or require disclosure of marketing expenditures and pricing information. State and foreign laws may govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

Insurance Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, which will require additional expenditure above and beyond the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Current and future healthcare reform legislation

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. The Affordable Care Act includes provisions of importance to our potential product candidates that:

- created an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide point-of-sale-discounts off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. For example, various portions of the Affordable Care Act are currently facing legal and constitutional challenges in the Fifth Circuit Court of Appeals and the United States Supreme Court. Additionally, the current administration has issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices, and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the Affordable Care Act. It is unclear whether the Affordable Care Act will be overturned, repealed, replaced, or further amended. We cannot predict what effect further changes to the Affordable Care Act would have on our business.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief and Economic Security Act, or CARES Act, which was signed into law in March 2020 and is designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended these reductions from May 1, 2020 through December 31, 2020. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, including bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. For example, at the federal level, the current administration's budgets for fiscal years 2019 and 2020 contained further drug price control measures that could be enacted in future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the current administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Although a number of these and other measures may require additional authorization to become effective, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Additionally, in the United States, the Medicare Modernization Act, or MMA, contains provisions that call for the promulgation of regulations that expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U.S. importation laws will not take effect, unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of the HHS made such certification to Congress, and on October 1, 2020, FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. Since the issuance of the final rule, several industry groups have filed federal lawsuits challenging multiple aspects of the final rule, and authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. On September 25, 2020, CMS stated drugs imported by States under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed upon. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Compliance with other federal and state laws or requirements; changing legal requirements

If any products that we may develop are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, labeling, packaging, distribution, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws, among other requirements to which we may be subject.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive recordkeeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements may subject firms to legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, relabeling or repackaging, or refusal to allow a firm to enter into supply contracts, including government contracts. Any claim or action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on marketing, sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling or packaging; (iii) the recall or discontinuation of our products; or (iv) additional recordkeeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Other U.S. environmental, health and safety laws and regulations

We may be subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Government Regulation of Drugs Outside of the United States

To market any product outside of the U.S., we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization or identification of an alternate regulatory pathway, manufacturing, commercial sales and distribution of our products. For instance, in the United Kingdom and the European Economic Area, or the EEA (comprised of the 27 EU Member States plus Iceland, Liechtenstein and Norway), medicinal products must be authorized for marketing by using either the centralized authorization procedure or national authorization procedures.

- *Centralized procedure*—If pursuing marketing authorization of a product candidate for a therapeutic indication under the centralized procedure, following the opinion of the European Medicines Agency’s Committee for Medicinal Products for Human Use, or, CHMP, the European Commission issues a single marketing authorization valid across the EEA. The centralized procedure is compulsory for human medicines derived from biotechnology processes or advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), products that contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases, and officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the European Medicines Agency, or EMA, as long as the medicine concerned contains a new active substance not yet authorized in the EEA, is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the EEA. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops.
- *National authorization procedures*—There are also two other possible routes to authorize products for therapeutic indications in several countries, which are available for products that fall outside the scope of the centralized procedure:
 - *Decentralized procedure*—Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.
 - *Mutual recognition procedure*—In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, additional marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

In the EEA, new products for therapeutic indications that are authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The criteria for designating an “orphan medicinal product” in the EEA are similar in principle to those in the U.S. In the EEA a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year orphan market exclusivity period, no marketing authorization application shall be accepted, and no marketing authorization shall be granted for a similar medicinal product for the same indication. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

Similar to as in the U.S., the various phases of non-clinical and clinical research in the European Union are subject to significant regulatory controls.

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific trial site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will apply following confirmation of full functionality of the Clinical Trials Information System, or CTIS, the centralized European Union portal and database for clinical trials foreseen by the regulation, through an independent audit. The regulation becomes applicable six months after the European Commission publishes notice of this confirmation. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial. The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union.

The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, the “EU portal”; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

Government regulation of data collection outside of the United States

In the event we conduct clinical trials in the European Union, we will be subject to additional privacy restrictions. The collection and use of personal health data in the European Economic Area, or EEA (being the European Union plus Norway, Iceland, and Liechtenstein), is governed by the General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR applies to the processing of personal data by any company established in the EEA and to companies established outside the EEA to the extent they process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, requirements to conduct privacy impact assessments for “high risk” processing, limitations on retention of personal data, mandatory data breach notification and “privacy by design” requirements, and creates direct obligations on service providers acting as processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the United States (which, while deemed a third country, has the benefit of the Privacy Shield regime for transatlantic data transfers). Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States and Norway, Iceland and Liechtenstein, which may deviate slightly from the GDPR, may result in fines of up to 4% of a company’s global revenues for the preceding financial year, or €20,000,000, whichever is greater. Moreover, the GDPR grants data subjects the right to claim material and non-material damages resulting from infringement of the GDPR. Given the breadth and depth of changes in data protection obligations, maintaining compliance with the GDPR will require significant time, resources and expense, and we may be required to put in place additional controls and processes ensuring compliance with the new data protection rules. There has been limited enforcement of the GDPR to date, particularly in biopharmaceutical development, so we face uncertainty as to the exact interpretation of the new requirements on any future trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law. Further, the United Kingdom’s decision to leave the European Union, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated now that the United Kingdom has left the European Union.

There is significant uncertainty related to the manner in which data protection authorities will seek to enforce compliance with GDPR. For example, it is not clear if the authorities will conduct random audits of companies doing business in the EU, or if the authorities will wait for complaints to be filed by individuals who claim their rights have been violated. Enforcement uncertainty and the costs associated with ensuring GDPR compliance are onerous and may adversely affect our business, financial condition, results of operations and prospects.

Should we utilize third party distributors, compliance with such foreign governmental regulations would generally be the responsibility of such distributors, who may be independent contractors over whom we have limited control.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, in March 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom formally left the European Union on January 31, 2020. A transition period began on February 1, 2020, during which European Union pharmaceutical law remains applicable to the United Kingdom. This transition period is due to end on December 31, 2020. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Employees and Human Capital

As of December 31, 2020, we had 75 full-time employees, of which 46 have M.D. or Ph.D. degrees. Within our workforce, 54 employees are engaged in research and development and 21 are engaged in business development, finance, legal, and general management and administration. We consider the intellectual capital of our employees to be an essential driver of our business and key to our future prospects. Our workforce expanded during FY20; new employees were hired to support and extend our clinical and preclinical pipeline, with hires in commercial, clinical development and operations, research, manufacturing, and general and administrative functions. We expect to continue to add additional employees in 2021 with a focus on expanding increasing expertise and bandwidth in clinical and preclinical research and development. The Company continually evaluates the business need and opportunity and balances in house expertise and capacity with outsourced expertise and capacity. Currently, the Company outsources substantial all clinical trial work to clinical research organizations and certain drug manufacturing to contract manufacturers. Drug development is a complex endeavor which requires deep expertise and experience across a broad array of disciplines. Pharmaceutical companies both large and small compete for a limited number qualified applicants to fill specialized positions. We monitor our compensation programs closely and provide what we consider to be a very competitive mix of compensation and insurance benefits for all our employees, as well as participation in our equity programs. To attract qualified applicants, the Company offers a total rewards package consisting of base salary and cash target bonus, a comprehensive benefit package and equity compensation for every employee. Bonus opportunity and equity compensation increase as a percentage of total compensation based on level of responsibility. Actual bonus payout is based on performance.

None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relations with our employees to be good.

We support our employees' further development with individualized development plans, mentoring, coaching, group training, conference attendance and financial support including tuition reimbursement.

Response to COVID-19

Beginning in March 2020, we have supported our employees and government efforts to curb the COVID-19 pandemic through a multifaceted communication, infrastructure, and behavior modification and enforcement effort:

- Establishing clear and regular COVID-19 policies, safety protocols, and updates to all employees;
- Decrease density and increasing physical distancing in workspaces for employees working onsite by scheduling adjustments and adding work from home flexibility;
- Adjusting attendance policies to encourage those who are sick to stay home;
- Increasing cleaning protocols at our Watertown, MA headquarters;
- Providing additional personal protective equipment and cleaning supplies;
- Implemented weekly COVID-19 testing;
- Implementing protocols to address actual and suspected COVID-19 cases and potential exposure;
- Prohibiting all domestic and international non-essential travel for all employees;
- Requiring masks to be worn in all locations; and
- Established a subsidy to support employees during COVID-19

Facilities

Our corporate headquarters are located in Watertown, Massachusetts, where we lease and occupy approximately 34,522 square feet of office and laboratory space. The current term of our Watertown lease expires March 31, 2030, with an option to extend the term five additional years with 12 months' notice with rent set at an agreed upon market rate.

Our existing facilities are sufficient to meet our current needs. To meet the future needs of our business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 1A. Risk Factors.

Our business involves a high degree of risk. You should carefully consider the material and other risks and uncertainties described and summarized below, as well as the other information in this Annual Report on Form 10-K, including our consolidated financial statements and related notes and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Special Note Regarding Forward-Looking Statements,” before you make an investment decision. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K. The risks described below are not the only risks that we face. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. As a result, the market price of our common stock could decline, and you may lose all or part of your investment in our common stock.

Risks Related to Our Financial Position and Need for Additional Capital

We are a biopharmaceutical company with a limited operating history and have not generated any revenue to date from drug sales, and may never become profitable.

Biopharmaceutical drug development is a highly speculative undertaking and involves a substantial degree of risk. Since our formation in 2015 and our initial funding in 2016, our operations to date have been limited primarily to organizing and staffing our company, business planning, raising capital, researching and developing our drug discovery technology, developing our pipeline, building our intellectual property portfolio, undertaking preclinical studies of our product candidates and initiating a Phase 1 first-in-human clinical trial of KT-474, a highly active and selective, orally bioavailable IRAK4 degrader. We have never generated any revenue from drug sales. We have not obtained regulatory approvals for any of our current or future product candidates.

Typically, it takes many years to develop one new pharmaceutical drug from the time it is discovered to when it is available for treating patients. Consequently, any predictions we make about our future success or viability may not be as accurate as they could be if we had a longer operating history. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors, such as the COVID-19 pandemic. We will need to transition from a company with a research and development focus to a company capable of supporting late-stage development and commercial activities. We may not be successful in such a transition.

We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

Since inception, we have focused substantially all of our efforts and financial resources on developing our proprietary targeted protein degradation drug discovery platform, or the Pegasus platform, and initial product candidates as well as supporting our collaborations and partnerships. To date, we have financed our operations primarily through the issuance and sale of our convertible preferred stock to outside investors and collaborators in private equity financings, upfront payments under our existing collaborations and our initial public offering. From our inception through December 31, 2020, we raised an aggregate of \$617.8 million of gross proceeds from such transactions and through our collaborations with Genzyme Corporation, or Sanofi and Vertex Pharmaceuticals Incorporated, or Vertex. As of December 31, 2020, our cash and cash equivalents and investments were \$458.7 million. We have incurred net losses in each year since our inception, and we had an accumulated deficit of \$128.8 million as of December 31, 2020. For the years ended December 31, 2020 and 2019, we reported net losses of \$45.6 million and \$41.2 million, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders’ deficit and working capital. We expect our expenses to significantly increase in connection with our ongoing activities, as we:

- initiate and complete clinical trials for current or future product candidates, including the ongoing Phase 1 trial of KT-474;
- prepare and submit Investigational New Drug applications, or INDs, with the U.S. Food and Drug Administration, or FDA, for KT-413, a highly active and selective, IRAKIMiD degrader and other current and future product candidates;
- prepare and submit Investigational New Drug applications, or INDs, with the U.S. Food and Drug Administration, or FDA, for KT-333, a highly active and selective STAT3 degrader and other current and future product candidates;

- develop and scale up our capabilities to support our ongoing preclinical activities and clinical trials for our product candidates and commercialization of any of our product candidates for which we may obtain marketing approval;
- secure facilities to support continued growth in our research, development and commercialization efforts;
- advance research and development related activities to expand our product pipeline;
- expand and improve the capabilities of our Pegasus platform;
- seek regulatory approval for our product candidates that successfully complete clinical development;
- contract to manufacture our product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific and management personnel; and
- incur additional costs associated with continuing to operate as a public company.

In addition, if we obtain marketing approval for our current or future product candidates, we will incur significant expenses relating to sales, marketing, product manufacturing and distribution. Because of the numerous risks and uncertainties associated with developing pharmaceutical drugs, including in light of the ongoing evolution of the COVID-19 pandemic, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Risks Related to Future Financial Condition

We will need to raise substantial additional funding. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, scale back or discontinue some of our product candidate development programs or future commercialization efforts.

The development of pharmaceutical drugs is capital-intensive. We are currently advancing multiple development candidates through preclinical development across a number of potential indications and, in the first quarter of 2021, commenced clinical development of KT-474. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue the research and development of, advance the preclinical and clinical activities of, and seek marketing approval for, our current or future product candidates. In addition, if we obtain marketing approval for any of our current or future product candidates, we expect to incur significant commercialization expenses related to sales, marketing, product manufacturing and distribution to the extent that such sales, marketing, product manufacturing and distribution are not the responsibility of our collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our current or future product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, scale back or discontinue the development and commercialization of one or more of our product candidates, and may be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

As of December 31, 2020, we had approximately \$458.7 million of cash and cash equivalents and investments. On August 25, 2020, we completed an initial public offering of our common stock by issuing 9,987,520 shares of our common stock, including the exercise in full by the underwriters of their option to purchase up to 1,302,720 additional shares of common stock, at a public offering price of \$20.00 per share. The aggregate gross proceeds to the Company from the offering, before deducting underwriting discounts and commissions, and other estimated offering expenses payable by the Company, were approximately \$199.8 million. Concurrent with the initial public offering, the Company announced the sale of 676,354 common shares at the public offering price per share in a private placement to Vertex. The aggregate gross proceeds to the Company from the concurrent private placement were approximately \$13.5 million. The concurrent private placement also closed on August 25, 2020. We expect that the approximately \$458.7 million of cash and cash equivalents and investments at December 31, 2020 will be sufficient to fund our operations into 2025. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate also assumes that we do not obtain any additional funding through collaborations or other strategic alliances. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our current or future product candidates, including additional expenses attributable to adjusting our development plans (including any supply related matters) in response to the COVID-19 pandemic;

- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our current or future product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any existing or additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other current or future product candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory clearances to market our current or future product candidates.

Identifying potential current or future product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our current or future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional funding to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current or future product candidates. Disruptions in the financial markets in general may make equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms favorable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or current or future product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which require, among other things, that we file with the Securities and Exchange Commission, or the SEC, annual quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as “say on pay” and proxy access. Emerging growth companies may implement many of these requirements over a longer period and up to five years from the pricing of our initial public offering. We intend to take advantage of these extended transition periods, but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies substantially increase our legal and financial compliance costs and make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

Risks Related to Drug Development and Regulatory Approval

Risks Related to Preclinical and Clinical Development

We are very early in our development efforts. All of our product candidates are in preclinical or early clinical development. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

Our ability to become profitable depends upon our ability to generate revenue. To date, while we have generated collaboration revenue, we have not generated any revenue from our product candidates, and we do not expect to generate any revenue from the sale of drugs in the near future. We do not expect to generate revenue from product sales unless and until we complete the development of, obtain marketing approval for, and begin to sell, one or more of our product candidates. We are also unable to predict when, if ever, we will be able to generate revenue from such product candidates due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- the results of the single ascending dose, or SAD, portion of the Phase 1 trial of KT-474 in healthy volunteers;
- our plans to initiate enrollment of the multiple ascending dose, or MAD, portion of the Phase 1 trial of KT-474, which is currently on partial clinical hold pending FDA review and clearance of interim data from the SAD portion of the trial, in healthy volunteers in the second half of 2021;
- submitting INDs to the FDA for KT-413, KT-333 and other current or future product candidates;
- our successful initiation, enrollment of and completion of clinical trials for other current and future product candidates, including our ability to generate positive data from any such clinical trials;
- our ability to receive regulatory approvals from applicable regulatory authorities;
- the initiation and successful completion of all safety studies required to obtain U.S. and foreign marketing approval for our product candidates;
- the costs associated with the development of any additional development programs we identify in-house or acquire through collaborations or other arrangements;
- our ability to establish manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- obtaining and maintaining acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- the success of our existing collaborations as well as the terms and timing of any additional collaboration, license or other arrangement, including the terms and timing of any payments thereunder;
- our ability to enforce and defend intellectual property rights and claims; and
- our ability maintain a continued acceptable safety profile of our product candidates following approval.

We expect to incur significant sales and marketing costs as we prepare to commercialize our current or future product candidates. Even if we initiate and successfully complete pivotal or registration-enabling clinical trials of our current or future product candidates, and our current or future product candidates are approved for commercial sale, and despite expending these costs, our current or future product candidates may not be commercially successful. We may not achieve profitability soon after generating drug sales, if ever. If we are unable to generate revenue, we will not become profitable and may be unable to continue operations without continued funding.

Our approach to the discovery and development of product candidates based on our Pegasus platform is novel and unproven, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any products.

Our Pegasus platform utilizes a method known as targeted protein degradation, or TPD, to discover and develop product candidates. Our future success depends on the successful development of this novel therapeutic approach. No product candidates using TPD have been approved in the United States or Europe, and the data underlying the feasibility of developing such therapeutic products is both preliminary and limited. In addition, we have not yet succeeded and may not succeed in demonstrating the efficacy and safety of any of our product candidates in clinical trials or in obtaining marketing approval thereafter. In particular, our ability to successfully achieve TPD with a therapeutic result requires the successful development of heterobifunctional molecules that were intentionally designed with a rational drug development process and developing those molecules with the right combination of protein targets and E3 ligases. This is a complex process requiring a number of component parts or biological mechanisms to work in unison to achieve the desired effect. We cannot be certain that we will be able to discover degraders by matching the right target with the ideal E3 ligase and the right linker in a timely manner, or at all. We have recently initiated a first-in-human Phase 1 clinical trial of KT-474, but we have not yet assessed safety of any other product candidates in humans. As such, there may be adverse effects from treatment with any of our current or future product candidates that we cannot predict at this time.

As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our Pegasus platform, or any similar or competitive platforms, will result in the development and marketing approval of any products. Any development problems we experience in the future related to our Pegasus platform or any of our research programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Any of these factors may prevent us from completing our preclinical studies and clinical trials or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

We may not be successful in our efforts to identify or discover additional product candidates or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

A key element of our strategy is to apply our Pegasus platform and product pipeline to address a broad array of targets and new therapeutic areas. The therapeutic discovery activities that we are conducting may not be successful in identifying product candidates that are useful in treating oncology, inflammation, immunology or genetic diseases. Our research programs may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Because we have limited financial and management resources, we focus on a limited number of research programs and product candidates. We are currently focused on our three most advanced development programs IRAK4, IRAKIMiD, and STAT3, which target key signaling pathways implicated in multiple inflammatory and autoimmune diseases as well as numerous cancers. As a result, we may forego or delay pursuit of opportunities with other current or future product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and current or future product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We depend heavily on the successful development of our lead programs. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, any of our current or future product candidates.

We currently have no product candidates approved for sale and may never be able to develop marketable product candidates. Our business depends heavily on the successful development, regulatory approval and commercialization of our current or future product candidates, including our IRAK4, IRAKIMiD, and STAT3 programs. The preclinical studies and clinical trials of our current or future product candidates are, and the manufacturing and marketing of our current or future product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to test or, if approved, market any of our current or future product candidates. Before obtaining regulatory approvals for the commercial sale of any of our current or future product candidates, we must demonstrate through preclinical studies and clinical trials that each product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our preclinical studies and clinical trials. This process can take many years and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources. Of the large number of drugs in development in the U.S., only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized, with similarly low rates of success for drugs in development in the European Union obtaining regulatory approval from the European Medicines Agency, or EMA. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and preclinical studies and clinical trials, we cannot assure you that any of our current or future product candidates will be successfully developed or commercialized. For example, in December 2020, we submitted an IND application for KT-474 to initiate a first-in-human Phase 1 randomized, double-blind, placebo-controlled clinical trial in healthy volunteers and patients with hidradenitis suppurativa (HS) or atopic dermatitis (AD). We were notified by the FDA that we may initiate dosing of healthy volunteers in the SAD portion of the Phase 1 clinical trial and that the program is on partial clinical hold regarding the MAD portion of the Phase 1 trial, pending FDA review of interim data in healthy volunteers from the SAD portion of the trial. We cannot be certain that the FDA will lift the partial clinical hold on KT-474 for the MAD portion of the Phase 1 trial to proceed which could negatively impact the future clinical development of KT-474.

We are not permitted to market our current or future product candidates in the U.S. until we receive approval of a New Drug Application, or an NDA, from the FDA, in the European Economic Area, or EEA, until we receive approval of a marketing authorization application, or an MAA, from the EMA, or in any other foreign countries until we receive the requisite approval from such countries. Obtaining approval of an NDA or MAA is a complex, lengthy, expensive and uncertain process, and the FDA or EMA may delay, limit or deny approval of any of our current or future product candidates for many reasons, including, among others:

- we may not be able to demonstrate that our current or future product candidates are safe and effective in treating their target indications to the satisfaction of the FDA or applicable foreign regulatory agency;
- the results of our preclinical studies and clinical trials may not meet the level of statistical or clinical significance required by the FDA or applicable foreign regulatory agency for marketing approval;
- the FDA or applicable foreign regulatory agency may disagree with the number, design, size, conduct or implementation of our preclinical studies and clinical trials;
- the FDA or applicable foreign regulatory agency may require that we conduct additional preclinical studies and clinical trials;
- the FDA or applicable foreign regulatory agency may not approve the formulation, labeling or specifications of any of our current or future product candidates;
- the contract research organizations, or CROs, that we retain to conduct our preclinical studies and clinical trials may take actions outside of our control that materially adversely impact our preclinical studies and clinical trials;
- the FDA or applicable foreign regulatory agency may find the data from preclinical studies and clinical trials insufficient to demonstrate that our current or future product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or applicable foreign regulatory agency may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA or applicable foreign regulatory agency may not accept data generated at our preclinical studies and clinical trial sites;
- if our NDA, if and when submitted, is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

- the FDA may require development of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or post-approval;
- the FDA or the applicable foreign regulatory agency may determine that the manufacturing processes or facilities of third-party manufacturers with which we contract do not conform to applicable requirements, including current Good Manufacturing Practices, or cGMPs;
- the FDA or applicable foreign regulatory agency may be delayed in its review processes due to staffing or other constraints arising from the COVID-19 pandemic; or
- the FDA or applicable foreign regulatory agency may change its approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market our current or future product candidates. Any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

If we experience delays or difficulties in the initiation or enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

There may be delays in trial initiation, and we may not be able to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the U.S. In particular, our ability to open clinical sites and enroll patients may be significantly delayed by the evolving COVID-19 pandemic and we do not know the extent and scope of such delays at this point. Moreover, some of our competitors have ongoing clinical trials for current or future product candidates that treat the same patient populations as our current or future product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' current or future product candidates.

Patient enrollment may be affected by other factors including:

- the size and nature of the patient population;
- competition with other companies for clinical sites or patients;
- the willingness of participants to enroll in our clinical trials in our countries of interest;
- the severity of the disease under investigation;
- the eligibility criteria for the clinical trial in question;
- the availability of an appropriate screening test for the indications we are pursuing;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in and completion of clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients; and
- factors we may not be able to control, such as potential pandemics that may limit subjects, principal investigators or staff or clinical site availability (e.g., the outbreak of COVID-19).

Interim, "topline," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final

data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their diseases. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, results of operations, prospects or financial condition.

The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

The precise incidence and prevalence for the indications being pursued by our current and future product candidates are currently unknown. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. We are developing KT-474 for the treatment of a broad set of immunology-inflammation diseases, such as HS, an inflammatory skin disease, AD, and rheumatoid arthritis. The total addressable market opportunity for our product candidates will ultimately depend upon, among other things, their proven safety and efficacy, the diagnosis criteria included in the final label for each, whether our product candidates are approved for sale for these indications, acceptance by the medical community and patient access, product pricing and reimbursement. The number of patients for our product candidates in the United States and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidate.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. In December 2019, a novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes COVID-19, surfaced in Wuhan, China and has since spread worldwide, including to Eastern Massachusetts where our primary office and laboratory space is located. The coronavirus pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. The extent to which the coronavirus impacts our operations or those of our third-party partners, including our preclinical studies or clinical trial operations, will also depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, new information that will emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among others. The continued spread of COVID-19 globally could adversely impact our preclinical or clinical trial operations in the U.S. and abroad, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19. For example, similar to other biopharmaceutical companies, we may experience delays in enrolling the MAD portion of our Phase 1 clinical trial for KT-474, which is currently planned for the second half of 2021. COVID-19 may also affect employees of third-party CROs located in affected geographies that we rely upon to carry out our clinical trials. In addition, the patient populations that our lead and other core product candidates target may be particularly susceptible to COVID-19, which may make it more difficult for us to identify patients able to enroll in our clinical trials and may impact the ability of enrolled patients to complete any such trials. Any negative impact COVID-19 has to patient enrollment or treatment or the execution of our product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

Additionally, timely enrollment in clinical trials is dependent upon clinical trial sites which will be adversely affected by global health matters, such as pandemics. We are conducting and plan to conduct clinical trials for our product candidates in geographies which are currently being affected by the coronavirus. Some factors from the coronavirus outbreak that will delay or otherwise adversely affect enrollment in the clinical trials of our product candidates, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials;
- limitations on travel that could interrupt key trial and business activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, including any government-imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our clinical trial sites or secure visas or entry permissions, a loss of face-to-face meetings and other interactions with potential partners, any of which could delay or adversely impact the conduct or progress of our clinical trials;
- the potential negative affect on the operations of our third-party manufacturers and the supply chain for our product candidates. For example, in February 2020, one of our vendors for active pharmaceutical ingredient, or API, starting materials based in Wuhan, China ceased its operations for several weeks due to the COVID-19 pandemic, which caused a minor delay in the delivery of API starting materials to a separate vendor who manufactures API;
- interruptions in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product and conditioning drugs and other supplies used in our current and prospective clinical trials; and
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

We have taken temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring part or all of our employees to work remotely, suspending all non-essential travel worldwide for our employees and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business. We cannot presently predict the scope and severity of the planned and potential shutdowns or disruptions of businesses and government agencies, such as the SEC or FDA. For example, since March 2020, foreign and domestic inspections by the FDA have largely been on hold with the FDA announcing plans in July 2020 to resume prioritized domestic inspections. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

These and other factors arising from the coronavirus could worsen. Any of these factors, and other factors related to any such disruptions that are unforeseen, could have a material adverse effect on our business and our results of operations and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize our product candidates.

Our current or future product candidates may cause adverse or other undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

We have initiated a first-in-human Phase 1 clinical trial of KT-474, but have not evaluated any other product candidates in human clinical trials. Undesirable side effects caused by our current or future product candidates could cause us to interrupt, delay or halt preclinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. As is the case with many treatments for inflammatory and autoimmune diseases, cancer or other diseases, it is likely that there may be adverse side effects associated with the use of our product candidates. Additionally, a potential risk in any protein degradation product is that healthy proteins or proteins not targeted for degradation will be degraded or that the degradation of the targeted protein in itself could cause adverse events, undesirable side effects, or unexpected characteristics. It is possible that healthy proteins or proteins not targeted for degradation could be degraded using our degrader molecules in any of our current or future clinical studies. There is also the potential risk of delayed adverse events following treatment using any of our current or future product candidates.

These side effects could arise due to off-target activity, allergic reactions in trial subjects, or unwanted on-target effects in the body. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our current or future product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our current or future product candidates could cause undesirable side effects in clinical trials related to on-target toxicity. If on-target toxicity is observed, or if our current or future product candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in early-stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further development of the compound.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our current or future product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our current or future product candidates receive marketing approval and we or others identify undesirable side effects caused by such current or future product candidates after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such current or future product candidates;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such current or future product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the current or future product candidates;
- regulatory authorities may require a REMS plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such current or future product candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our current or future product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our current or future product candidates, if approved, and significantly impact our ability to successfully commercialize our current or future product candidates and generate revenues.

Positive results from early preclinical studies and clinical trials of our current or future product candidates are not necessarily predictive of the results of later preclinical studies and clinical trials of our current or future product candidates. If we cannot replicate the positive results from our preclinical studies of our current or future product candidates in our future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our current or future product candidates.

Positive results from our preclinical studies of our current or future product candidates, and any positive results we may obtain from our early clinical trials of our current or future product candidates, may not necessarily be predictive of the results from required later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies or clinical trials of our current or future product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our current or future product candidates may not be replicated in subsequent preclinical studies or clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings

made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain approval from the FDA or comparable foreign regulatory authority. If we fail to produce positive results in our planned preclinical studies or clinical trials of any of our current or future product candidates, the development timeline and regulatory approval and commercialization prospects for our current or future product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Additionally, our planned or future clinical trials may utilize an “open-label” trial design. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

Manufacturing our current or future product candidates is complex and we may encounter difficulties in production. If we encounter such difficulties, our ability to provide supply of our current or future product candidates for preclinical studies and clinical trials or for commercial purposes could be delayed or stopped.

The process of manufacturing our current or future product candidates is complex and highly regulated.

We do not have our own manufacturing facilities or personnel and currently rely, and expect to continue to rely, on third parties for the manufacture of our current or future product candidates. These third-party manufacturing providers may not be able to provide adequate resources or capacity to meet our needs and may incorporate their own proprietary processes into our product candidate manufacturing processes. We have limited control and oversight of a third party’s proprietary process, and a third party may elect to modify its process without our consent or knowledge. These modifications, such as any impacting the product formulation, could negatively impact our manufacturing, including by resulting in product loss or failure that requires additional manufacturing runs or a change in manufacturer, either of which could significantly increase the cost of and significantly delay the manufacture of our current or future product candidates. Changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

As our current or future product candidates progress through preclinical studies and clinical trials towards potential approval and commercialization, it is expected that various aspects of the manufacturing process will be altered in an effort to optimize processes and results. Such changes may require amendments to be made to regulatory applications which may further delay the timeframes under which modified manufacturing processes can be used for any of our current or future product candidates and additional bridging studies or trials may be required. Any such delay could have a material adverse impact on our business, results of operations and prospects.

Risks Related to Regulatory Approval

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our current or future product candidates, we will not be able to commercialize, or will be delayed in commercializing, our current or future product candidates, and our ability to generate revenue will be materially impaired.

Our current or future product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import, and export, are subject to comprehensive regulation by the FDA and other regulatory agencies in the U.S. and by comparable authorities in other countries. Before we can commercialize any of our current or future product candidates, we must obtain marketing approval from the regulatory authorities in the relevant jurisdictions. We have not received approval to market any of our current or future product candidates from regulatory authorities in any jurisdiction, and it is possible that none of our current product candidates, nor any product candidates we may seek to develop in the future, will ever obtain regulatory approval. As a company, we have only limited experience in filing and supporting the applications necessary to gain

regulatory approvals and expect to rely on third-party CROs and/or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities and often clinical sites by, the relevant regulatory authority. Our current or future product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining regulatory approvals, both in the U.S. and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted NDA or equivalent application type outside the U.S., may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our current or future product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our current or future product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

As of June 23, 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals; however, the FDA may not be able to continue its current pace and review timelines could be extended. In addition, even if we were to obtain approval, regulatory authorities may approve any of our current or future product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our current or future product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our current or future product candidates, the commercial prospects for our current or future product candidates may be harmed and our ability to generate revenues will be materially impaired.

Breakthrough Therapy Designation and Fast Track Designation by the FDA, even if granted for any of our current or future product candidates, may not lead to a faster development, regulatory review or approval process, and such designations do not increase the likelihood that any of our product candidates will receive marketing approval in the United States.

We may seek a Breakthrough Therapy Designation for one or more of our current or future product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our current or future product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a current or future product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our current or future product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We may seek Fast Track Designation for one or more of our current or future product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular current or future product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation for certain current or future product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track Designation alone does not guarantee qualification for the FDA's priority review procedures.

We may seek Orphan Drug Designation for certain of our current or future product candidates, and we may be unsuccessful or may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity.

As part of our business strategy, we may seek Orphan Drug Designation for certain indications of our current or future product candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the U.S. and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the U.S., Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Similarly, in Europe, the European Commission, upon the recommendation of the EMA's Committee for Orphan Medicinal Products, grants Orphan Drug Designation to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in Europe and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in Europe would be sufficient to justify the necessary investment in developing the drug. In Europe, Orphan Drug Designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a product with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the U.S. and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a drug no longer meets the criteria for Orphan Drug Designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan Drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain Orphan Drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because competing drugs containing a different active ingredient can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, the U.S. Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where the FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its Orphan Drug regulations and policies, our business could be adversely impacted.

Even if we receive regulatory approval for any of our current or future product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our current or future product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates when and if any of them are approved.

If the FDA or a comparable foreign regulatory authority approves any of our current or future product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the drug will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration requirements, and continued compliance with cGMPs and Good Clinical Practices, or GCPs, for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our current or future product candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug. Later discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, or voluntary drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of drug license approvals;
- drug seizure or detention, or refusal to permit the import or export of drugs; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our current or future product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Risks Related to Foreign Regulatory Approval and Foreign Markets

Even if we receive marketing approval for our current or future product candidates in the U.S., we may never receive regulatory approval to market our current or future product candidates outside of the U.S.

We plan to seek regulatory approval of our current or future product candidates outside of the U.S. In order to market any product outside of the U.S., however, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ substantially from that required to obtain FDA approval. The marketing approval processes in other countries generally implicate all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. In particular, in many countries outside of the U.S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our current or future product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that could materially adversely affect our business.

We are not permitted to market or promote any of our current or future product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our current or future product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our current or future product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our current or future product candidates and ultimately commercialize our current or future product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- differing regulatory requirements in foreign countries, such that obtaining regulatory approvals outside of the U.S. may take longer and be more costly than obtaining approval in the U.S.;
- our customers' ability to obtain reimbursement for our current or future product candidates in foreign markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;

- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

Foreign sales of our current or future product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

We may in the future conduct clinical trials for current or future product candidates outside the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We may in the future choose to conduct one or more clinical trials outside the U.S., including in Europe. The acceptance of study data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which we collectively refer to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In addition, many countries outside the U.S. have limited government support programs that provide for reimbursement of drugs such as our product candidates, with an emphasis on private payors for access to commercial products. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Even if we are able to commercialize any current or future product candidates, such drugs may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the U.S. and in other countries, sales of any products for which we may receive regulatory marketing approval for commercial sale will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government healthcare programs (e.g., Medicare and Medicaid), managed care providers, private health insurers, health maintenance organizations and other organizations. These third-party payors decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and other third-party payors is essential for most patients to be able to afford treatments such as targeted protein degradation therapies.

In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Our ability to commercialize any current or future product candidates successfully also will depend in part on the extent to which coverage and reimbursement for these current or future product candidates and related treatments will be available from government authorities, private health insurers and other organizations. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. We cannot be sure that coverage will be available for any product candidate that we commercialize. If coverage is available, but reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

In the U.S., no uniform policy exists for coverage and reimbursement for products among third-party payors. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate a payor will pay for the product. One third-party payor's decision to cover a particular product or service does not ensure that other payors will also provide coverage for the medical product or service. Third-party payors may limit coverage to specific products on an approved list or formulary, which may not include all FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded product on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Further, third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Despite our best efforts, our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition.

Finally, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing product pricing vary widely from country to country. For example, in the EU pricing and reimbursement of pharmaceutical products are regulated at a national level under the individual EU Member States' social security systems. Some foreign countries provide options to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost

effectiveness of a particular product candidate to currently available therapies. A country may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Even if approved for reimbursement, historically, product candidates launched in some foreign countries, such as some countries in the EU, do not follow price structures of the U.S. and prices generally tend to be significantly lower.

Current and future healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States and in some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes intended to broaden access to healthcare, improve the quality of healthcare, and contain or lower the cost of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, expands the types of entities eligible for the 340B drug discount program, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been judicial, administrative, executive and Congressional legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, various portions of the ACA are currently undergoing constitutional challenges in the U.S. Supreme Court, the Trump Administration has issued various Executive Orders eliminating cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices, and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. Specifically, the Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, and subsequent legislation, the 2% Medicare sequester reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the pandemic. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The BBA also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and has further resulted in proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, at the federal level, the Trump administration's budget for fiscal year 2021 includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the Trump Administration previously released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of product candidates paid by consumers. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions after January 20, 2021. HHS has solicited feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

Additionally, former President Trump signed a series of Executive Orders on July 24, 2020 and September 13, 2020 aimed at lowering drug pricing and seeking to implement several of the administration's proposals. The FDA also released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. The Interim Final Rule has not been finalized and is subject to revision and challenge. Additionally, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our current or future product candidates or additional pricing pressures. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our relationships with customers, health care providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished future profits and earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any current or future product candidates for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors and customers may expose us to broadly applicable federal and state laws relating to fraud and abuse, as well as other healthcare laws and regulations. These laws may impact, among other things, the business or financial arrangements and relationships through which we market, sell and distribute any current or future product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, among others:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully soliciting, offering, receiving, providing or paying remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, or arranging for, any item, good, facility, or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations can result in significant civil monetary and criminal penalties for each violation, plus up to three times the amount of remuneration, imprisonment, and exclusion from government healthcare programs. Further, a violation of the federal Anti-Kickback Statute can also form the basis for False Claims Act liability;
- the federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which prohibits individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in very significant monetary penalties for each false claim and three times the amount of the government's damages. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes additional criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal physician payment transparency laws, including the federal Physician Payment Sunshine Act created under the ACA, which requires manufacturers of certain drugs, devices, biologics and medical supplies, among others, to track and disclose payments under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) and other transfers of value they make to U.S. physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. This information is subsequently made publicly available in a searchable format on a CMS website. Failure to disclose required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, including the final omnibus rule published on January 25, 2013, which imposes, among other things, certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain, transmit, or obtain, protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions; and
- analogous state law equivalents of each of the above U.S. federal laws, such as state anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state and local marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require the reporting of information related to drug pricing; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; state and local laws that require the licensure and/or registration of pharmaceutical sales representatives; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

In addition to the above, on November 20, 2020, the Office of Inspector General, or OIG, finalized further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. The final rule (with some exceptions) became effective January 19, 2021. We continue to evaluate what effect, if any, these rules will have on our business.

It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties, and sanctions.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading laws.

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the U.S. and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing, patient support and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Other activities subject to these laws include the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, reputational harm, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Risks Related to Commercialization

Even if we receive marketing approval for our current or future product candidates, our current or future product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales.

The commercial success of our current or future product candidates, if approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance of our current or future product candidates among the medical community, including physicians, patients and healthcare payors. Market acceptance of our current or future product candidates, if approved, will depend on a number of factors, including, among others:

- the efficacy of our current or future product candidates as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for the applicable indications, to provide patients with incremental health benefits, as compared with other available medicines;
- limitations or warnings contained in the labeling approved for our current or future product candidates by the FDA or other applicable regulatory authorities;
- the clinical indications for which our current or future product candidates are approved;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the potential and perceived advantages of our current or future product candidates over current treatment options or alternative treatments, including future alternative treatments;
- the willingness of the target patient population to try new therapies or treatment methods and of physicians to prescribe these therapies or methods;
- the need to dose such product candidates in combination with other therapeutic agents, and related costs;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of our current or future product candidates;
- our ability to obtain sufficient third-party coverage or reimbursement; or
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If our current or future product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from our current or future product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our current or future product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community, patient organizations and third-party payors about the benefits of our current or future product candidates may require significant resources and may never be successful.

We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We face and will continue to face competition from third parties that use protein degradation, antibody therapy, inhibitory nucleic acid, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization of new drugs.

Competitors in our efforts to develop small molecule protein degraders therapies for patients, include, but are not limited to, Arvinas, Inc. and C4 Therapeutics, Inc., which are both in clinical development, Nurix Therapeutics, Inc., Foghorn Therapeutics, Inc., and Vividion Therapeutics, Inc., each of which is in preclinical development. Further, several large pharmaceutical companies have disclosed preclinical investments in this field. Our competitors will also include companies that are or will be developing other targeted protein degradation methods as well as small molecule, antibody, or gene therapies for the same indications that we are targeting. In addition to the competitors we face in developing small molecule protein degraders, we will also face competition in the indications we expect to pursue with our IRAK4, IRAKIMiD and STAT3 programs. Many of these indications already have approved standards of care which may include more traditional therapeutic modalities. In order to compete effectively with these existing therapies, we will need to demonstrate that our protein degrader therapies are favorable to existing therapeutics.

Many of our current or future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and reimbursement and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our current or future product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any current or future product candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of our current or future product candidates in human clinical trials and will face an even greater risk if we commercially sell any current or future product candidates that we may develop. If we cannot successfully defend ourselves against claims that our current or future product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any current or future product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any current or future product candidates that we may develop.

We do not yet maintain product liability insurance, and we anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain product liability insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If, in the future, we are unable to establish sales and marketing and patient support capabilities or enter into agreements with third parties to sell and market our current or future product candidates, we may not be successful in commercializing our current or future product candidates if and when they are approved, and we may not be able to generate any revenue.

We do not currently have a sales or marketing infrastructure and have no experience in the sales, marketing, patient support or distribution of drugs. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, patient support, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our current or future product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing and patient support capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any drug launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our current or future product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing, patient support and distribution services, our drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any current or future product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our current or future product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our current or future product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our current or future product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct preclinical studies, and we expect to rely on third parties to conduct our clinical trials for our current and future product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialize our current and potential future product candidates and our business could be substantially harmed.

We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, contract manufacturing organizations and strategic partners to help conduct our preclinical studies. We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, contract laboratories, and other third parties, including collaboration partners, to conduct or otherwise support clinical trials for our current or future product candidates. We rely heavily on these parties for execution of clinical trials for our product candidates and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our preclinical studies or clinical trials, we could be subject to untitled and warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and any third parties that we contract with are required to comply with regulations and requirements, including GCP, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces GCP requirements through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or the third parties we contract with fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials will comply with GCP. In addition, our clinical trials must be conducted with current or future product candidates produced under cGMP regulations. Our failure or the failure of third parties that we may contract with to comply with these regulations may require us to repeat some aspects of a specific, or an entire, clinical trial, which would delay the marketing approval process and could also subject us to enforcement action. We also are required to register certain ongoing clinical trials and provide certain information, including information relating to the trial's protocol, on a government-sponsored database, ClinicalTrials.gov, within specific timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we designed the Phase 1 trial of KT-474 and intend to design other clinical trials for our current or future product candidates, or be involved in the design when other parties sponsor the trials, we anticipate that third parties will conduct all of our clinical trials. As a result, many important aspects of our clinical development, including their conduct, timing and response to the ongoing COVID-19 pandemic, will be outside of our direct control. Our reliance on third parties to conduct clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues; and
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If our CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, marketing approval and commercialization of our current or future product candidates may be delayed, we may not be able to obtain marketing approval and commercialize our current or future product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. If our CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain are compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain marketing approval for or successfully commercialize our current or future product candidates. As a result, we believe that our financial results and the commercial prospects for our current or future product candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

The third parties upon whom we rely for the supply of the API, drug product, and starting materials used in our product candidates are limited in number, and the loss of any of these suppliers could significantly harm our business.

The drug substance and drug product in our product candidates are supplied to us from a small number of suppliers, and in some cases sole source suppliers. Our ability to successfully develop our current or future product candidates, and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the drug product and drug substance for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing. We do not currently have arrangements in place for a redundant or second-source supply of all drug product or drug substance in the event any of our current suppliers of such drug product and drug substance cease their operations for any reason. Any delays in the delivery of our drug substance, drug product or starting materials could have an adverse effect and potentially harm our business. For example, in February 2020, one of our vendors for API starting materials based in Wuhan, China ceased its operations for several weeks due to the COVID-19 pandemic, which caused a minor delay in the delivery of API starting materials to a separate vendor who manufactures API.

For all of our current or future product candidates, we intend to identify and qualify additional manufacturers to provide such API, drug product and drug substance prior to submission of an NDA to the FDA and/or an MAA to the EMA. We are not certain, however, that our single-source and dual source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

Establishing additional or replacement suppliers for the drug product and drug substance used in our current or future product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the drug product and drug substance used in our current or future product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such API, drug product and drug substance from alternate sources at acceptable prices in a timely manner, could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

Our success is dependent on our executive management team's ability to successfully pursue business development, strategic partnerships and investment opportunities as our company matures. We may also form or seek strategic alliances or acquisitions or enter into additional collaboration and licensing arrangements in the future, and we may not realize the benefits of such collaborations, alliances, acquisitions or licensing arrangements.

We have entered into collaboration and licensing arrangements with Vertex and Sanofi and may in the future form or seek strategic alliances or acquisitions, create joint ventures, or enter into additional collaboration and licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our current product candidates and any future product candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or acquisition or other alternative arrangements for our current or future product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our current or future product candidates as having the requisite potential to demonstrate safety, potency, purity and efficacy and obtain marketing approval.

Further, collaborations involving our technologies or current or future product candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our current or future product candidates or may elect not to continue or renew development or commercialization of our current or future product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our current or future product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;

- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our current or future product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates. For example, the collaboration agreement with Vertex may be terminated by Vertex either in its entirety or on a target-by-target basis, upon one hundred eighty days' prior written notice to us, upon our material breach, subject to specified notice and cure provisions, or upon our bankruptcy, insolvency, dissolution or winding up;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property; and
- collaborators may not pay milestones and royalties due to the company in a timely manner.

As a result, we may not be able to realize the benefit of our existing collaboration and licensing arrangements or any future strategic partnerships or acquisitions, collaborations or license arrangements we may enter into if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction, license, collaboration or other business development partnership, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our current or future product candidates could delay the development and commercialization of our current or future product candidates in certain geographies or for certain indications, which would harm our business prospects, financial condition and results of operations.

Our manufacturing process needs to comply with FDA regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our preclinical and clinical programs and suspension or withdrawal of any regulatory approvals.

In order to commercially produce our products either at our own facility or at a third party's facility, we will need to comply with the FDA's cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We are subject to inspections by the FDA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging, or storage of our product candidates as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our current or future product candidates, including leading to significant delays in the availability of our product candidates for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our current or future product candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our current or future product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical materials, by our third-party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the U.S. governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

Risks Related to Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for our technology and product candidates or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired, and we may not be able to compete effectively in our market.

Our commercial success depends in part on our ability to obtain and maintain patent or other intellectual property protection in the U.S. and other countries for our current or future product candidates and our core technologies, including our proprietary Pegasus platform, our initial IRAK4, IRAK1MiD, and STAT3 programs, which are our three most advanced development programs, as well as our proprietary compound library and other know-how. We seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the U.S. and abroad related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We own patent applications related to our platform E3 ligase ligand technology and our novel bifunctional degrader compounds, including claims to compositions of matter, pharmaceutical compositions, methods of use, methods of treatment, and other related methods.

As of December 31, 2020, our patent portfolio covering novel compounds discovered by our Pegasus platform included 43 patent families. Patent term adjustments, supplementary protection certificate filings, or patent term extensions could result in later expiration dates in various countries, while terminal disclaimers could result in earlier expiration dates in the U.S.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation.

The degree of patent protection we require to successfully commercialize our current or future product candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our pending patent applications that mature into issued patents will include claims with a scope sufficient to protect our Pegasus platform and our current or future product candidates. In addition, if the breadth or strength of protection provided by our patent applications or any patents we may own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. For example, in jurisdictions outside the U.S., a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Accordingly, any actual or purported co-owner of our patent rights could seek monetary or equitable relief requiring us to pay it compensation for, or refrain from, exploiting these patents due to such co-ownership. Furthermore, patents have a limited lifespan. In the U.S., and most other jurisdictions in which we have undertaken patent filings, the natural expiration of a patent is generally twenty years after it is filed, assuming all maintenance fees are paid. Various extensions may be available, on a jurisdiction-by-jurisdiction basis; however, the life of a patent, and thus the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, patents we may own or in-license may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our current or future product candidates, including generic versions of such drugs.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same compounds, methods, formulations or other subject matter, in either case that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until at least 18 months after the earliest priority date of the patent filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in patents we may own or in-license patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty.

In addition, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Further, with respect to certain pending patent applications covering our current or future product candidates or technologies, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the relevant patent office(s) may be significantly narrowed by the time they issue, if they ever do. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to establish and/or maintain a competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the U.S. and abroad. We may become involved in opposition, derivation, reexamination, *inter partes* review, or post-grant review proceedings challenging our patent rights or the patent rights of others from whom we may in the future obtain licenses to such rights, in the U.S. Patent and Trademark Office, or USPTO, the European Patent Office, or EPO, or in other countries. In addition, we may be subject to third-party submissions to the USPTO, the EPO, or elsewhere, that may reduce the scope or preclude the granting of claims from our pending patent applications. Competitors may challenge our issued patents or may file patent applications before we do. Competitors may also claim that we are infringing their patents and that we therefore cannot practice our technology as claimed under our patents or patent applications. Competitors may also contest our patents by showing an administrative patent authority or judge that the invention was not patent-eligible, was not novel, was obvious, and/or lacked inventive step, and/or that the patent application failed to meet relevant requirements relating to description, basis, enablement, and/or support; in litigation, a competitor could assert that our patents are not valid or are unenforceable for a number of reasons. If a court or administrative patent authority agrees, we would lose our protection of those challenged patents.

An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, without payment to us, or could limit the duration of the patent protection covering our technology and current or future product candidates. Such challenges may also result in our inability to manufacture or commercialize our current or future product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our proprietary know-how, information or technology to assign or grant similar rights to their inventions to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy.

Even if they are unchallenged, our issued patents and our pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent patents we may own or in-license by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third party may develop a competitive drug that provides benefits similar to one or more of our current or future product candidates but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our current or future product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our current or future product candidates could be negatively affected, which would harm our business.

Furthermore, even if we are able to issue patents with claims of valuable scope in one or more jurisdictions, we may not be able to secure such claims in all relevant jurisdictions, or in a sufficient number to meaningfully reduce competition. Our competitors may be able to develop and commercialize their products, including products identical to ours, in any jurisdiction in which we are unable to obtain, maintain, or enforce such patent claims.

We will not obtain patent or other intellectual property protection for all current or future product candidates in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

We may not be able to pursue patent coverage of our current or future product candidates, the Pegasus platform, or other technologies in all countries. Filing, prosecuting and defending patents on current or future product candidates, the Pegasus platform, and other technologies in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from infringing on our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the U.S. These products may compete with our current or future product candidates and in jurisdictions where we do not have any issued patents our patent applications or other intellectual property rights may not be effective or sufficient to prevent them from competing. Much of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to pharmaceutical products, which could make it difficult for us to stop the infringement of any patents we may own or in-license or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce any rights we may have in our patent applications or any patents we may own or in-license in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put any patents we may own or in-license at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents we may own or license that are relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

We may not obtain or grant licenses or sublicenses to intellectual property rights in all markets on equally or sufficiently favorable terms with third parties.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. The licensing of third-party intellectual property rights is a competitive area, and more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. More established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected current or future product candidates, which could materially harm our business, and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. Any of the foregoing could harm our competitive position, business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in our current or any future agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are dependent on patents, know-how and proprietary technology, both our own and in-licensed from Vertex, Sanofi and other collaborators. Our commercial success depends upon our ability to develop, manufacture, market and sell our current or future product candidates and use our and our licensors' proprietary technologies without infringing the proprietary rights of third parties. Vertex, Sanofi and other collaborators may have the right to terminate their respective license agreements in full in the event that we materially breach or default in the performance of any of the obligations under such license agreements.

Any termination of these licenses, or if the underlying patents fail to provide the intended exclusivity, could result in the loss of significant rights and could harm our ability to commercialize our current or future product candidates, the Pegasus platform, or other technologies, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours, and we may be required to cease our development and commercialization of certain of our current or future product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Disputes may also arise between us and our current or future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our current or future product candidates, and what activities satisfy those diligence obligations;
- the priority of invention of any patented technology; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners.

In addition, the agreements under which we may license intellectual property or technology from third parties are likely to be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we may license prevent or impair our ability to maintain current or future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected current or future product candidates or technologies, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Intellectual property rights do not guarantee commercial success of current or future product candidates or other business activities. Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- patent applications that we own or may in-license may not lead to issued patents;
- patents, should they issue, that we may own or in-license, may not provide us with any competitive advantages, may be narrowed in scope, or may be challenged and held invalid or unenforceable;

- others may be able to develop and/or practice technology, including compounds that are similar to the chemical compositions of our current or future product candidates, that is similar to our technology or aspects of our technology but that is not covered by the claims of any patents we may own or in-license, should any patents issue;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we, or our future licensors or collaborators, might not have been the first to make the inventions covered by a patent application that we own or may in-license;
- we, or our future licensors or collaborators, might not have been the first to file patent applications covering a particular invention;
- others may independently develop similar or alternative technologies without infringing, misappropriating or otherwise violating our intellectual property rights;
- our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not be able to obtain and/or maintain necessary licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights, or any rights at all, over that intellectual property;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such trade secrets or know-how;
- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Risks Related to Patent Protection

Obtaining and maintaining our patent protection, including patent term, depends on compliance with various procedural, document submission, deadlines, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we miss a filing deadline for patent protection on these inventions or otherwise fail to comply with these requirements.

The USPTO and foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after issuance of any patent. In addition, periodic maintenance fees, renewal fees, annuity fees and/or various other government fees are required to be paid periodically. While an inadvertent lapse can in some cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market with similar or identical products or platforms, which could have a material adverse effect on our business prospects and financial condition.

Depending upon the timing, duration and specifics of FDA marketing approval of our current or future product candidates, one or more of the U.S. patents we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Different laws govern the extension of patents on approved pharmaceutical products in Europe and other jurisdictions. However, we may not be granted a patent extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension in the U.S. if all of our patents covering an approved product expire more than fourteen years from the date of NDA approval for a product covered by those patents. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our current or future product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the U.S. and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Risks Related to our Trademarks, Trade Names and Trade Secrets

If our trademarks and trade names for our products or company name are not adequately protected in one or more countries where we intend to market our products, we may delay the launch of product brand names, use different trademarks or tradenames in different countries, or face other potentially adverse consequences to building our product brand recognition.

Our trademarks or trade name may be challenged, infringed, diluted, circumvented, declared generic, or determined to be infringing on other marks. In such a circumstance, we may not be able to protect our rights to these marks or may be forced to stop using product names, which we need for name recognition by potential partners and customers in our markets of interest.

In addition, during the trademark registration process, we may receive Office Actions from the USPTO or from comparable agencies in foreign jurisdictions refusing registration of our trademarks. In the USPTO and in comparable agencies in many foreign jurisdictions, third parties are also given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. For example, in November 2019, Novartis AG filed actions in the U.S. and European Union trademark offices opposing our applications to register KYMERA and KYMERA THERAPEUTICS for pharmaceuticals and drug development services on the basis of its claimed rights in the KYMIRIAH mark. This dispute was amicably settled in October 2020 and Kymera's pending applications for KYMERA and KYMERA THERAPEUTICS should proceed to registration in both jurisdictions. Opposition or cancellation proceedings may be filed against future trademark applications or registrations, and our trademark applications or registrations may not survive such proceedings. In the United States and other jurisdictions that recognize common law trademark rights, we intend to rely on both registration and common law protection for our trademarks. However, if we are unable to obtain registrations of future trademarks due to trademark office obstacles or third party objections, we may not be able to compete as effectively and our business may be adversely affected.

If we are unable to adequately protect and enforce our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents we may own or in-license, we seek to rely on trade secret protection, confidentiality agreements, and license agreements to protect proprietary know-how that may not be patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that may not be covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, trade secrets can be difficult to protect and we have limited control over the protection of trade secrets used by our collaborators and suppliers. We cannot be certain that we have or will obtain these agreements in all circumstances and we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary information.

Moreover, any of these parties might breach the agreements and intentionally or inadvertently disclose our trade secret information and we may not be able to obtain adequate remedies for such breaches. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Furthermore, the laws of some foreign countries do not protect proprietary rights and trade secrets to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition, results of operations and future prospects.

In the case of employees, we enter into agreements providing that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. Although we require all of our employees to assign their inventions to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Intellectual Property Litigation and Infringement Claims

We may initiate, become a defendant in, or otherwise become party to lawsuits to protect or enforce our intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe any intellectual property we may own or in-license, including our patents and trademarks. In addition, any intellectual property we may own or in-license also may become the subject of a dispute, including those based on inventorship, priority, validity or unenforceability. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that any intellectual property we may own or in-license is not valid or is unenforceable or that the other party's use of our technology that may be patented falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). There is also the risk that, even if the validity of these patents is upheld, the court may refuse to stop the other party from using the technology at issue on the grounds that any patents we may own or in-license do not cover the technology in question or that such third party's activities do not infringe our patent applications or any patents we may own or in-license. An adverse result in any litigation or defense proceedings could put one or more of any patents or other intellectual property we may own or in-license at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our own applications at risk of not issuing. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, patient support or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Post-grant proceedings provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our patent applications or any patents we may own or in-license. These proceedings are expensive and an unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition to potential USPTO post-grant proceedings, we may become a party to patent opposition proceedings in the EPO, or similar proceedings in other foreign patent offices or courts where our patents may be challenged. The costs of these proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result in a post-grant challenge proceeding may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business. Litigation or post-grant proceedings within patent offices may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may not be able to detect infringement against any intellectual property we may own or in-license. Even if we detect infringement by a third party of any intellectual property we may own or in-license, we may choose not to pursue litigation against or settlement with the third party. If we later sue such third party for infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce any patents or other intellectual property we may own or in-license against such third party.

Intellectual property litigation and administrative office challenges in one or more countries could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, patient support or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. As noted above, some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace, including compromising our ability to raise the funds necessary to continue our preclinical studies and future clinical trials, continue our research programs, license necessary technology from third parties, or enter into development collaborations that would help us commercialize our current or future product candidates, if approved. Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

We may be subject to damages or settlement costs resulting from claims that we or our employees have violated the intellectual property rights of third parties, or are in breach of our agreements. We may be accused of, allege or otherwise become party to lawsuits or disputes alleging wrongful disclosure of third-party confidential information by us or by another party, including current or former employees, contractors or consultants. In addition to diverting attention and resources, such disputes could adversely impact our business reputation and/or protection of our proprietary technology.

The intellectual property landscape relevant to our products and programs is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability to develop, manufacture, market and sell our current and future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including derivation, interference, reexamination, *inter partes* review and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We or any of our current or future licensors or strategic partners may be party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that our current or future product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. We cannot assure you that our current or future product candidates, the Pegasus platform, and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties. For example, many of our employees were previously employed at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees, consultants and advisors, even those related to one or more of our current or future product candidates, the Pegasus platform, or other technologies, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims.

While certain activities related to development and preclinical and clinical testing of our current or future product candidates may be subject to safe harbor of patent infringement under 35 U.S.C. §271(e)(1), upon receiving FDA approval for such candidates we or any of our future licensors or strategic partners may immediately become party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that such product candidates infringe, misappropriate or otherwise violate their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our current or future product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our current or future product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our current or future product candidates, technologies or methods.

If a third party claims that we infringe, misappropriate or otherwise violate its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement, misappropriation and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business and may impact our reputation;
- substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our current or future product candidates, or from using our proprietary technologies, including our Pegasus platform, unless the third-party licenses its product rights to us, which it is not required to do on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products, or the license to us may be non-exclusive, which would permit third parties to use the same intellectual property to compete with us;
- redesigning our current or future product candidates or processes so they do not infringe, misappropriate or violate third-party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; and
- there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Some of our competitors may be able to sustain the costs of litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

Third parties may assert that we are employing their proprietary technology without authorization. Patents issued in the U.S. by law enjoy a presumption of validity that can be rebutted in U.S. courts only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our current or future product candidates. Patent applications can take many years to issue. In addition, because some patent applications in the U.S. may be maintained in secrecy until the patents are issued, patent applications in the U.S. and many foreign jurisdictions are typically not published until 18 months after their earliest priority filing date, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications covering our current or future product candidates or technology. If any such patent applications issue as patents, and if such patents have priority over our patent applications or patents we may own or in-license, we may be required to obtain rights to such patents owned by third parties which may not be available on commercially reasonable terms or at all, or may only be available on a non-exclusive basis. There may be currently pending third-party patent applications which may later result in issued patents that our current or future product candidates may infringe. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our current or future product candidates or other technologies, could be found to be infringed by our current or future product candidates or other technologies. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our current or future product candidates, molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our current or future product candidates or Pegasus platform may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be nonexclusive, thereby giving our competitors access to the same technologies licensed to us.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our current or future product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement, misappropriation or other violation against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our current or future product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our current or future product candidates or technologies, which could harm our business significantly.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might subject us to infringement claims or adversely affect our ability to develop and market our current or future product candidates.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending patent application in the U.S. and abroad that is relevant to or necessary for the commercialization of our current or future product candidates in any jurisdiction. For example, U.S. patent applications filed before November 29, 2000 and certain U.S. patent applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. As mentioned above, patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our current or future product candidates could have been filed by third parties without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our current or future product candidates or the use of our current or future product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our current or future product candidates. We may incorrectly determine that our current or future product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the U.S. or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our current or future product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our current or future product candidates.

If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, which may be significant, we may be temporarily or permanently prohibited from commercializing any of our current or future product candidates or technologies that are held to be infringing. We might, if possible, also be forced to redesign current or future product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business and could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical and business development expertise of Nello Mainolfi, Ph.D., our President and Chief Executive Officer, Jared Gollob, M.D., our Chief Medical Officer, Bruce Jacobs, our Chief Financial Officer, and Richard Chesworth, DPhil, our Chief Scientific Officer, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of December 31, 2020, we had 75 full-time employees, and we will continue to increase our number of employees and the scope of our operations. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our current or future product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our current or future product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

We or the third parties upon whom we depend may be adversely affected by natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, including any potential effects from the current global spread of COVID-19, power shortage, telecommunication failure or other natural or man-made accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Natural disasters or pandemics such as the COVID-19 outbreak could further disrupt our operations, and have a material and adverse effect on our business, financial condition, results of operations and prospects. For example, we have instituted a temporary work from home policy for non-essential office personnel and it is possible that this could have a negative impact on the execution of our business plans and operations. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure our investors that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities or the manufacturing facilities of our third-party contract manufacturers are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Data and Privacy

Our internal computer systems, or those of our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our current or future product candidates' development programs.

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of data from preclinical studies or clinical trials for our current or future product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, other data or applications relating to our technology or current or future product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our current or future product candidates could be delayed.

We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (*e.g.*, state breach notification laws), federal (*e.g.*, HIPAA, as amended by HITECH), and international law (*e.g.*, the EU General Data Protection Regulation, or GDPR) and may cause a material adverse impact to our reputation, affect our ability to use collected data, conduct new studies and potentially disrupt our business.

We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. We also rely on our employees and consultants to safeguard their security credentials and follow our policies and procedures regarding use and access of computers and other devices that may contain our sensitive information. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above, as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business.

Risks Related to Our Common Stock

The price of our common stock may be volatile and fluctuate substantially, and you may lose all or part of your investment.

Our stock price is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may lose all or part of your investment. The market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;
- results of preclinical studies and clinical trials of our current or future product candidates or those of our competitors;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our current or future product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional current or future product candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

COVID-19 has been spreading rapidly around the world since December 2019 and has negatively affected the stock market and investor sentiment. The price of our common stock may be disproportionately affected as investors may favor traditional profit-making industries and companies during the times of market uncertainty and instability.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability, including most recently in connection with the COVID-19 pandemic. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or current or future product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect your rights as a common stockholder. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or current or future product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, scale back or discontinue the development and commercialization of one or more of our product candidates, delay our pursuit of potential in-licenses or acquisitions or grant rights to develop and market current or future product candidates that we would otherwise prefer to develop and market ourselves.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Our executive officers, directors, principal stockholders and their affiliates exercise significant influence over our company, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

The existing holdings of our executive officers, directors, principal stockholders and their affiliates will represent beneficial ownership, in the aggregate, of approximately 36% of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, upon the expiration of the lock-up agreements, the early release of these agreements, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock.

All shares of common stock sold in our initial public offering or otherwise outstanding as of our initial public offering are able to be sold in the public market. Shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market standoff and lock-up agreements, and Rule 144 and Rule 701 under the Securities Act.

Certain holders of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also filed a registration statement on Form S-8 registering the issuance of 9.5 million shares of common stock issued or reserved for future issuance under our equity compensation plans. Shares registered under this registration statement on Form S-8 can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described above. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Risks Related to Tax

Changes in tax law may adversely affect us or our investors.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made and changes are likely to continue to occur in the future.

For example, the Tax Cuts and Jobs Act, or the TCJA, was enacted in 2017 and made significant changes to corporate taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses from taxable years beginning after December 31, 2017 to 80% of current year taxable income and the elimination of net operating loss carrybacks generated in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), and the modification or repeal of many business deductions and credits. In addition, on March 27, 2020, former President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, which, among other things, suspends the 80% limitation on the deduction for net operating losses in taxable years beginning before January 1, 2021, permits a 5-year carryback of net operating losses arising in taxable years beginning after December 31, 2017 and before January 1, 2021, and generally caps the limitation on the deduction for net interest expense at 50% of adjusted taxable income for taxable years beginning in 2019 and 2020.

It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be subject to certain limitations, and, as a result, unavailable to reduce our future tax liability.

As of December 31, 2020, we had federal and state net operating loss carryforwards of \$74.4 million and \$61.2 million, respectively, which begin to expire in various amounts in 2036 (other than federal net operating loss carryforwards arising in taxable years beginning after December 31, 2017, which are not subject to expiration). As of December 31, 2020, we also had federal and state research and development tax credit carryforwards of \$2.7 million and \$1.3 million, respectively, which begin to expire in 2036. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change

net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who own at least 5% of a corporation's stock increases by more than 50 percentage points over the lowest ownership percentage of such stockholders or groups of stockholders within a specified testing period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes. Moreover, if we undergo any additional ownership changes, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating U.S. federal and state taxable income. As described above under "Risk Factors—Risks Related to our Financial Position and Need for Additional Capital," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; and therefore, we do not know whether or when we will generate the U.S. federal or state taxable income necessary to utilize our NOLs or credit carryforwards that are subject to limitation by Sections 382 and 383 of the Code.

Risks Related to Our Controls and Reporting Requirements

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we will need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell any of our present or future product candidates that may receive regulatory approval.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

We are an emerging growth company and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act, or JOBS Act, enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this Annual Report and our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder

approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the year in which we completed our initial public offering, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed \$700 million as of the prior June 30th, and (ii) the date on which we have issued more than \$1 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to not “opt out” of this exemption from complying with new or revised accounting standards and, therefore, we will adopt new or revised accounting standards at the time private companies adopt the new or revised accounting standard and will do so until such time that we either (i) irrevocably elect to “opt out” of such extended transition period or (ii) no longer qualify as an emerging growth company.

Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Risks Related to Our Charter and Bylaws

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our fourth amended and restated certificate of incorporation and our second amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, or DGCL, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These antitakeover provisions and other provisions in our fourth amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any state law claims for (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of or based on a breach of a fiduciary duty owed by any director, officer or other employee of ours to us or our stockholders; (3) any action asserting a claim pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; or (4) any action asserting a claim governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts, as applicable. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We currently occupy approximately 34,522 rentable square feet of office and laboratory space in Watertown, Massachusetts under a lease that expires in March 2030. We have an option to extend the lease term for five additional years. We believe that our office and laboratory space is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time, we may be subject to legal proceedings and claims in the ordinary course of business. We are not currently aware of any such proceedings or claims that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol “KYMR” on the Nasdaq Global Select Market and has been publicly traded since August 21, 2020. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of February 28, 2021, there were approximately 69 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in “nominee” or “street” name.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Recent Sales of Unregistered Securities

None.

Item 6. Selected Financial Data.

Reserved.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our audited financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis and set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the section titled "Risk Factors" in Part I, Item 1A of this Annual Report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on discovering and developing novel small molecule therapeutics that selectively degrade disease-causing proteins by harnessing the body's own natural protein degradation system. Our proprietary targeted protein degradation platform, which we refer to as Pegasus™, allows us to discover highly selective small molecule protein degraders with activity against disease-causing proteins throughout the body. We believe that our small molecule protein degraders have unique advantages over existing therapies and allow us to address a large portion of the human genome that was previously intractable with traditional modalities. We focus on biological pathways that have been clinically validated but where key biological nodes/proteins have not been drugged or inadequately drugged. To date, we have utilized our Pegasus™ platform to design novel protein degraders focused in the areas of immunology-inflammation and oncology, and continue to apply our platform's capabilities to additional therapeutic areas. Our initial programs are IRAK4, IRAKIMiD, and STAT3, which each address high impact targets within the interleukin-1 receptor/toll-like receptor, or IL-1R/TLR, and janus kinase/signal transducers and activators of transcription, or JAK/STAT, providing the opportunity to treat a broad range of immune-inflammatory diseases, hematologic malignancies, and solid tumors. Our programs exemplify our focus on addressing high impact targets that have been elusive to conventional modalities and that drive the pathogenesis of multiple serious diseases with significant unmet medical needs. With respect to our IRAK4 program, we are collaborating with Genzyme Corporation, a subsidiary of Sanofi S.A, or Sanofi, on the development of drug candidates targeting IRAK4 outside the oncology and immuno-oncology fields. We submitted an Investigational New Drug Application, or IND, to the U.S. Food and Drug Administration, or FDA, for KT-474 in 2020, and initiated the SAD portion of our Phase 1 trial in adult healthy volunteers in February 2021. We also expect to submit INDs for degraders from our IRAKIMiD and STAT3 programs in the second half of 2021, and if cleared, to initiate Phase 1 trials in patients thereafter.

Since our inception in 2015, we have devoted substantially all of our efforts to organizing and staffing our company, research and development activities, business planning, raising capital, building our intellectual property portfolio and providing general and administrative support for these operations. To date, we had received gross proceeds of \$617.8 million from the sale of common stock including our August 2020 initial public offering and concurrent private placement, sales of our convertible preferred stock and through our collaborations with Vertex Pharmaceuticals Incorporated, or Vertex, and Genzyme Corporation, or Sanofi.

We have incurred significant operating losses since inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current product candidates or any future product candidates. Our net losses were \$45.6 million and \$41.2 million for the years ended December 31, 2020 and 2019, respectively. In addition, as of December 31, 2020 and 2019 we had an accumulated deficit of \$128.8 million and \$76.5 million, respectively. We expect that our expense and capital requirements will increase substantially in connection with our ongoing activities, particularly if and as we:

- continue preclinical activities of our initial programs, IRAK4, IRAKIMiD and STAT3, including the advancement of our IRAK4 program into a Phase 1 Clinical Trial;
- initiate and continue research and preclinical and clinical development of our other product candidates;
- advance the development of our product candidate pipeline;
- continue to develop and expand our Pegasus platform to identify additional product candidates;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;
- acquire or in-license additional product candidates and technologies;

- expand our infrastructure and facilities to accommodate our growing employee base and ongoing development activity; and
- require the manufacture of larger quantities of our product candidates for clinical development and potential commercialization;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs, any future commercialization efforts and operating as a public company.

In addition, if we obtain marketing approval for any of our lead product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which may include collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, reduce or eliminate the development and commercialization of one or more of our product candidates.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain marketing approval for our drug candidates. The lengthy process of securing marketing approvals for new drugs requires the expenditure of substantial resources. Any delay or failure to obtain regulatory approvals would materially adversely affect our product candidate development efforts and our business overall. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2020, we had cash, cash equivalents and marketable securities of \$458.7 million. We believe the existing cash, cash equivalents and marketable securities on hand, will enable us to fund our operating expenses and capital expenditure requirements into 2025. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See “—Liquidity and capital resources.”

Since it was reported to have surfaced in December 2019, a novel strain of coronavirus, Sars-Cov-2 which leads to COVID-19, has spread across the world and has been declared a pandemic by the World Health Organization. Efforts to contain the spread of COVID-19 have intensified and governments around the world, including in the United States, Europe and Asia, have implemented severe travel restrictions, social distancing requirements, stay-at-home orders and have delayed the commencement of non-COVID-19-related clinical trials, among other restrictions. As a result, the current COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, patients, communities and business operations, as well as contributing to significant volatility and negative pressure on the U.S. economy and in financial markets. We expect that COVID-19 precautions will directly or indirectly impact the timeline for some of our planned clinical trials and are continuing to assess the potential impact of the COVID-19 pandemic on our current and future business and operations, including our expenses and clinical trials, as well as on our industry and the healthcare system.

As a result of the outbreak, many companies have experienced disruptions in their operations and in markets served. To date, we have instated some and may take additional temporary precautionary measures intended to help ensure our employees’ well-being and minimize business disruption. These measures include devising contingency plans and securing additional resources from third-party service providers. For the safety of our employees and their families, we have temporarily reduced the presence of our scientists in our labs and continue to rely on third parties to conduct many of the experiments and studies for our research programs. Certain of our third-party service providers have also experienced shutdowns or other business disruptions. We are continuing to assess the impact of the COVID-19 pandemic on our current and future business and operations, including our expenses and planned clinical trial and other development timelines, as well as on our industry and the healthcare system.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. Our only revenues have been derived from research collaboration arrangements with Vertex and Sanofi. We expect that our revenue for the next several years will be derived primarily from our current collaboration agreements and any additional collaborations that we may enter into in the future. To date, we have not received any royalties under any of the collaboration agreements.

Vertex Collaboration Agreement

On May 9, 2019, we entered into a collaboration agreement, or the Vertex Agreement, with Vertex, to advance small molecule protein degradation against up to six targets. Under the Vertex Agreement, Vertex has the exclusive option to license the rights to the product candidates developed through the collaboration at which point Vertex will control development and commercialization. Pursuant to the Vertex Agreement, we are responsible for discovery and preclinical research on the targets, and Vertex is responsible for development, manufacturing, and commercialization of the product candidates after it exercises its option to license.

Vertex provided us with a non-refundable upfront payment of \$50.0 million and purchased 3,059,695 shares of our Series B-1 convertible preferred stock at \$6.54 a share, pursuant to a separate, but simultaneously executed Share Purchase Agreement. We are eligible to receive up to \$170 million in payments per target, including development, regulatory, and commercial milestones, as well as option exercise payments. In addition, Vertex is obligated to pay us tiered royalties on future net sales on any products that may result from the Vertex Agreement. None of the payments under the Vertex Agreement are refundable. We may also perform follow-on research activities for an optioned target upon Vertex's request and at Vertex's expense.

Sanofi Agreement

On July 7, 2020, we entered into a collaboration agreement, or the Sanofi Agreement, with Sanofi to co-develop drug candidates directed to two biological targets. Under the Sanofi Agreement, we granted to Sanofi a worldwide exclusive license to develop, manufacture and commercialize certain lead compounds generated during the collaboration directed against IRAK4 and one additional undisclosed target in an undisclosed field of use. Such license is exercisable on a collaboration target-by-collaboration target basis only after a specified milestone. For compounds directed against IRAK4, the field of use includes diagnosis, treatment, cure, mitigation or prevention of any diseases, disorders or conditions, excluding oncology and immunoncology. We are responsible for discovery and preclinical research and conducting a phase 1 clinical trial for at least one degrader directed against IRAK4 plus up to three backup degraders. With respect to both targets, Sanofi is responsible for development, manufacturing, and commercialization of product candidates after a specified development milestone occurs with respect to each collaboration candidate.

We have an exclusive option, or Opt-In Right, exercisable on a collaboration target-by-collaboration target basis that will include the right to (i) to fund 50% of the United States development costs for collaboration products directed against such target in the applicable field of use and (ii) share equally in the net profits and net losses of commercializing collaboration products directed against such target in the applicable field of use in the United States. In addition, if we exercise the Opt-In Right, Sanofi will grant to us an exclusive option, applicable to each collaboration target, which upon exercise will allow us to conduct certain co-promotion activities in the field in the United States.

The Sanofi Agreement, unless earlier terminated, will expire on a product-by-product basis on the date of expiration of all payment obligations under the Sanofi Agreement with respect to such product. We or Sanofi may terminate the agreement upon the other party's material breach or insolvency or for certain patent challenges. In addition, Sanofi may terminate the agreement for convenience or for a material safety event upon advance prior written notice, and we may terminate the agreement with respect to any collaboration candidate if, following Sanofi's assumption of responsibility for the development, commercialization or manufacturing of collaboration candidates with respect to a particular target, Sanofi ceases to exploit any collaboration candidates directed to such target for a specified period.

In consideration for the exclusive licenses granted to Sanofi under the Sanofi Agreement, Sanofi made an upfront payment of \$150 million. In addition to the upfront payment, we are eligible to receive certain development milestone payments of up to \$1.48 billion in the aggregate, of which more than \$1.0 billion relates to the IRAK4 program, upon the achievement of certain developmental or regulatory events. We will be eligible to receive certain commercial milestone payments up to \$700 million in the aggregate, of which \$400 million relates to the IRAK4 program, which are payable upon the achievement of certain net sales thresholds. We will be eligible to receive tiered royalties for each program on net sales ranging from the high single digits to high teens, subject to low-single digits upward adjustments in certain circumstances.

Operating expenses

Our operating expenses since inception have consisted solely of research and development expenses and general and administrative expenses.

Research and development expenses

Research and development expenses consist primarily of costs incurred in connection with the discovery and development of targeted protein degradation therapeutics, including those in our initial programs, IRAK4, IRAKIMiD and STAT3. These research efforts and costs, which also support the development of, and enhancements to, our Pegasus platform, include external research costs, personnel costs, supplies, license fees and facility-related expenses. We expense research and development costs as incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and stock-based compensation expense, for employees engaged in research and development functions;
- expenses incurred under agreements with organizations that support our platform program development;
- contract manufacturing organizations, or CMOs, that are primarily engaged to provide drug substance and product for our preclinical research and development programs, nonclinical studies and other scientific development services;
- the cost of acquiring and manufacturing nonclinical trial materials, including manufacturing registration and validation batches;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance;
- costs related to compliance with quality and regulatory requirements; and
- payments made under third-party licensing agreements.

Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will increase substantially in connection with our planned clinical development activities in the near term and in the future. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of any future product candidates.

Our future clinical development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;

- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our product candidates;
- the phase of development of our product candidates; and
- the efficacy and safety profile of our product candidates.

The successful development and commercialization of product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the following:

- the timing and progress of nonclinical and clinical development activities;
- the number and scope of nonclinical and clinical programs we decide to pursue;
- the ability to raise necessary additional funds;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current development program and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of drug substance and drug product for use in production of our product candidates;
- our ability to establish and maintain agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if any of our product candidates are approved;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;
- our ability to obtain and maintain third-party insurance coverage and adequate reimbursement;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- the impact of competition with other products;
- the impact of any business interruptions to our operations, including the timing and enrollment of patients in our planned clinical trials, or to those of our manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis; and
- our ability to maintain a continued acceptable safety profile for our therapies following approval.

A change in the outcome of any of these variables with respect to the development of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any of our product candidates.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, corporate and business development, and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters, professional fees for accounting, auditing, tax and administrative consulting services, insurance costs, administrative travel expenses, marketing expenses and other operating costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support development of our product candidates and our continued research activities. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as legal, investor and public relations expenses associated with being a public company.

Other Income (Expense)

Interest income and expense, net

Interest income consists of interest earned on our invested cash balances.

Results of Operations

Comparison of years ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019:

	Year ended December 31,		Change
	2020	2019	
	(in thousands)		
Revenue—from related parties	\$ 34,034	\$ 2,934	\$ 31,100
Operating expenses:			
Research and development	62,105	37,158	24,947
General and administrative	18,233	7,981	10,252
Total operating expenses	80,338	45,139	35,199
Loss from operations	(46,304)	(42,205)	(4,099)
Interest income, net	711	959	(248)
Net loss	\$ (45,593)	\$ (41,246)	\$ (4,347)

Collaboration revenue

We recognize revenue under each of the Vertex Agreement and Sanofi Agreement based on our pattern of performance related to the respective identified performance obligation, which is the period over which we will perform research services under each of the Vertex Agreement and Sanofi Agreement.

Collaboration revenues were \$34.0 million for the year ended December 31, 2020, of which \$15.2 million and \$18.8 million were attributable to our collaboration agreements with Vertex and Sanofi, respectively. Collaboration revenue was \$2.9 million for the year ended December 31, 2019, all of which was attributable to our collaboration with Vertex.

Research and development expenses

The following table summarizes our research and development expenses for each period presented:

	Year ended December 31,		Change
	2020	2019	
	(in thousands)		
External research and development costs:			
IRAK4 and IRAKIMiD	\$ 20,186	\$ 13,478	\$ 6,708
STAT3	6,674	2,474	4,200
Other	12,579	8,822	3,757
Internal research and development costs	22,666	12,384	10,282
Total research and development expenses	\$ 62,105	\$ 37,158	\$ 24,947

Research and development expenses were \$62.1 million for the year ended December 31, 2020, compared to \$37.2 million for the year ended December 31, 2019. The increase of \$25.0 million was primarily due to higher direct expenses related lead optimization activities for our IRAK programs of \$6.7 million and STAT3 programs of \$4.2 million, as well as increased investment in our platform, exploratory programs, and Vertex collaboration of \$3.8 million. We also had a \$10.2 million increase in personnel, occupancy and related costs due to increases in employee headcount in the research and development functions.

General and administrative expenses

General and administrative expenses were \$18.2 million for the year ended December 31, 2020, compared to \$8.0 million for the year ended December 31, 2019. The increase was primarily due to an increase in legal and professional service fees and an increase in personnel, facility, occupancy and other expenses stemming from an increase in headcount to support our growth as a public company.

Other Income, Net

Other income, net was \$0.7 million for the year ended December 31, 2020, compared to \$1.0 million for the year ended December 31, 2019. The decrease in was primarily due to the prevailing interest rates in the respective periods.

Liquidity and capital resources

We have not yet generated any revenue from any product sales, and we have incurred significant operating losses since our inception. We have not yet commercialized any products and we do not expect to generate revenue from sales of products for several years, if at all. To date, we have funded our operations primarily with proceeds from our initial public offering, sale of our convertible preferred stock and collaboration agreements. To date, we had received gross proceeds of \$617.8 million from the sale of common stock in our August 2020 initial public offering and concurrent private placement, sales of our convertible preferred stock and through our collaborations with Vertex and Sanofi. As of December 31, 2020, we had cash and cash equivalents and marketable securities of \$458.7 million.

Cash flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
	2020	2019
	(in thousands)	
Cash provided by operating activities	\$ 88,130	\$ 17,905
Cash used in investing activities	(422,588)	(16,486)
Cash provided by financing activities	289,262	34,911
Net (decrease) increase in cash, cash equivalents and restricted cash	<u>\$ (45,196)</u>	<u>\$ 36,330</u>

Cash Flow from Operating Activities

During the year ended December 31, 2020, operating activities provided \$88.1 million of cash, primarily resulting from \$150.0 million of proceeds received under our collaboration agreement with Sanofi executed in July 2020. Cash provided by operating activities also includes an increase of accounts payable and accruals of \$6.7 million, an increase in net operating assets and liabilities of \$0.7 million, offset by our net loss of \$45.6 million adjusted for net non-cash items of \$8.9 million (primarily stock-based compensation, depreciation expense and amortization of premiums and discounts on securities).

During the year ended December 31, 2019, operating activities provided \$17.9 million of cash, resulting from the \$55.9 million in aggregate payments received in connection with the Vertex Agreement, including the premium paid on the Series B-1 convertible preferred stock purchase. Cash provided by operating activities also includes an increase of accounts payable and accruals of \$3.2 million, an increase of net operating lease right-of-use assets and liabilities of \$1.0 million offset by a net decrease of operating assets and liabilities of \$1.0 million and our net loss of \$41.2 million.

Cash Flow used in Investing Activities

During the year ended December 31, 2020, cash used in investing activities was \$422.6 million comprised of purchases of marketable securities of \$529.4 million and purchases of property and equipment of \$9.1 million offset by maturities of marketable securities of \$115.9 million.

During the year ended December 31, 2019, investing activities used \$16.5 million of cash, primarily due to \$16.0 million in purchases of marketable securities and \$0.5 million in purchases of property and equipment.

Cash Flow from Financing Activities

During the year ended December 31, 2020, net cash provided by financing activities was \$289.3 million, primarily consisting of \$183.1 million of net proceeds received in our August 2020 initial public offering, \$13.5 million from our August 2020 concurrent private placement, \$88.2 million of proceeds from our issuances of Series C convertible preferred stock in March 2020, net of issuance costs, and \$4.8 million of proceeds from the second closing of our Series B convertible preferred stock financing in January 2020, net of issuance costs.

During the year ended December 31, 2019, net cash provided by financing activities was \$34.9 million, which consisted of \$14.0 million of proceeds from our issuances of Series B-1 convertible preferred stock in May 2019, net of issuance costs, and \$21.2 million of proceeds from the second closing of our Series B convertible preferred stock financing in December 2019, net of issuance costs.

Future funding requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the later-stage clinical development of our product candidates. In addition, we expect to incur additional costs associated with operating as a public company.

Because of the numerous risks and uncertainties associated with the development of our product candidates and programs and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. The timing and amount of our operating expenditures will depend largely on:

- the initiation, progress, timing, costs and results of nonclinical studies and clinical trials for our product candidates or any future product candidates we may develop;
- our ability to maintain our relationships with Vertex and other key collaborators;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more nonclinical studies or clinical trials than those that we currently expect or change their requirements on studies that had previously been agreed to;
- the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- the effect of competing technological and market developments;
- the costs of continuing to grow our business, including hiring key personnel and maintaining or acquiring operating space;
- the degree of market acceptance of any approved product candidates, including product pricing, as well as product coverage and the adequacy of reimbursement by third-party payors;
- the cost of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the cost and timing of selecting, auditing and potentially validating a manufacturing site for commercial-scale manufacturing;
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval and that we determine to commercialize; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

We believe the existing cash, cash equivalents and marketable securities on enable us to fund our operating expenses and capital expenditure requirements into 2025. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. We expect that we will require additional funding to continue the clinical development of our IRAK4, IRAKIMiD and STAT3 programs, commercialize our product candidates if we receive regulatory approval, and pursue in-licenses or acquisitions of other product candidates. If we receive regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize our product candidates.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and marketing, distribution or licensing arrangements with third parties. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Other Commitments

During the year ending December 31, 2020, there have been no material changes to our contractual obligations and commitments outside the ordinary course of business.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles, or GAAP, in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing at the end of this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services.

To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, we perform the following five steps: (i) identification of the contract(s) with the customer, (ii) identification of the promised goods or services in the contract and determination of whether the promised goods or services are performance obligations, (iii) measurement of the transaction price, (iv) allocation of the transaction price to the performance obligations, and (v) recognition of revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer.

When optional goods or services are offered, we assess the options to determine whether the options grant the customer a material right. This determination includes whether the option is priced at an amount that the customer would not have received without entering into the contract. If we conclude the option conveys a material right, it is accounted for as a separate performance obligation. In identifying performance obligations in a contract, we identify those promises that are distinct. Promised goods or services are considered distinct when the customer can benefit from the goods or services on their own, or together with readily available resources, and the goods or services are separately identifiable from other promises in the contract. If a promise is not distinct, it is combined with other promises in the contract until the combined group of promises is capable of being distinct.

We estimate the transaction price based on the amount of consideration we expect to receive for transferring the promised goods or services in the contract. The consideration may include both fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, we evaluate the amount of the potential payments and the likelihood that the payments will be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price. For contracts that include sales-based royalties for licensed compounds, we recognize revenue at the date when the related sales occur. Finally, we determine whether the contract contains a significant financing component by analyzing the promised consideration relative to the standalone selling price of the promised goods and services and the timing of payment relative to the transfer of the promised goods and services. At each reporting date, we reassess the transaction price and probability of achievement of the performance obligations and the associated constraints on transaction price. If necessary, we adjust the transaction price, recording a cumulative catch-up based on progress for the amount that was previously constrained.

Revenue is recognized when (or as) control of a performance obligation is transferred to the customer. When combined performance obligations contain a promised license and related services or other promises, management judgment is required to determine the appropriate timing of revenue recognition. In doing so, we must identify the predominant promise or promises in the contract to determine whether revenue is recognized at a point in time or over time. If over time, we must determine the appropriate measure of progress. If a license is deemed to be the predominant promise in a performance obligation, we must determine the nature of the license, whether functional or symbolic intellectual property, to conclude whether point-in-time or over-time revenue recognition is most appropriate. The determination of functional or symbolic intellectual property requires an assessment of whether the customer is able to exploit and benefit from the license in its current condition, or if the utility of the license is dependent on or influenced by our ongoing activities or being associated with us.

At each reporting date, we calculate the measure of progress for the performance obligations transferred over time. The calculation generally uses an input measure based on costs incurred to-date relative to estimated total costs to complete the transfer of the performance obligation. The measurement of progress is then used to calculate the total revenue earned, including any cumulative catch-up adjustment.

Research and Development Contract Costs and Accruals

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors, including research laboratories, in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical studies; and
- CMOs in connection with drug substance and drug product formulation of preclinical studies.

We base the expense recorded related to external research and development on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs and CROs that supply, conduct and manage nonclinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Equity-Based Compensation Expense

We measure equity-based awards granted to employees, directors, and nonemployees based on their fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. The equity-based payments include stock options and grants of common stock, including common stock subject to vesting. The measurement date for equity awards is the date of grant, and equity-based compensation costs are recognized as expense over the requisite service period, which is the vesting period, on a straight-line basis. We have issued stock options and restricted stock with performance-based vesting conditions and record the expense for these awards if we conclude that it is probable that the performance condition will be achieved. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. Expected volatility is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information is available. We select companies with comparable characteristics to us with historical share price information that approximates the expected term of the equity-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period that approximates the calculated expected term of our stock options. We will continue to apply this method until a sufficient amount of historical information regarding the volatility of our stock price becomes available. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption. We use the simplified method, under which the expected term is presumed to be the midpoint between the vesting date and the end of the contractual term. We utilize this method due to lack of historical exercise data. The expected dividend yield is assumed to be zero as we have no current plans to pay any dividends on common stock. The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of our common stock on that same date.

JOBS Act Accounting Election

Under Section 107(b) of the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, an "emerging growth company" can delay the adoption of new or revised accounting standards until such time as those standards would apply to private companies. We have elected to avail ourselves of this exemption to delay adopting new or revised accounting standards until such time as those standards apply to private companies. However, where allowable we have early adopted certain standards as described in Note 2 of our consolidated financial statements. There are other exemptions and reduced reporting requirements provided by the JOBS Act that we are currently evaluating. For example, as an "emerging growth company," we are exempt from Sections 14A(a) and (b) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which would otherwise require us to (1) submit certain executive compensation matters to shareholder advisory votes, such as "say-on-pay," "say-on-frequency," and "golden parachutes;" and (2) disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of our chief executive officer's compensation to our median employee compensation. We also intend to rely on an exemption from the rule requiring us to provide an auditor's attestation report on our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We will continue to remain an "emerging growth company" until the earliest of the following: (1) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (2) the last day of the fiscal year in which our total annual gross revenue is equal to or more than \$1.07 billion; (3) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than \$250 million measured on the last business day of our second fiscal quarter, or our annual revenues are less than \$100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than \$700 million measured on the last business day of our second fiscal quarter.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form of money market funds and marketable securities and are invested in U.S. treasury or government obligations and corporate securities. However, because of the short-term nature of the duration of our portfolio and the low-risk profile of our investments, we believe an immediate 10% change in market interest rates would not be expected to have a material impact on the fair market value of our investments portfolio or on our financial condition or results of operations.

We are also exposed to market risk related to changes in foreign currency exchange rates. We contract with vendors that are located in Asia and Europe and certain invoices are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these arrangements. We do not currently hedge our foreign currency exchange rate risk. As of December 31, 2020, we had no significant liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the year ended December 31, 2020.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets as of December 31, 2020 and 2019	F-3
Consolidated Statements of Operations and Comprehensive Loss for the Years ended December 31, 2020 and 2019	F-4
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit) for the Years ended December 31, 2020 and 2019	F-5
Consolidated Statements of Cash Flows for the Years ended December 31, 2020 and 2019	F-7
Notes to Consolidated Financial Statements	F-9

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Kymera Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Kymera Therapeutics, Inc. (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material aspects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risk of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.
Boston, Massachusetts
March 11, 2021

KYMERA THERAPEUTICS, INC.
Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31,	
	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	\$ 31,004	\$ 76,015
Marketable securities (Note 4)	265,198	15,942
Accounts receivable—due from related parties	577	—
Contract assets—due from related parties	856	—
Prepaid expenses and other current assets	4,704	888
Total current assets	\$ 302,339	\$ 92,845
Marketable securities, non-current (Note 4)	162,531	—
Property and equipment, net (Note 6)	10,841	3,794
Right-of-use assets, operating leases	9,845	18,289
Other assets	30	—
Restricted cash	1,589	1,774
Total assets	\$ 487,175	\$ 116,702
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 4,368	\$ 3,276
Accrued expenses (Note 8)	10,330	4,568
Deferred revenue, current	92,552	23,349
Operating lease liabilities, current portion	2,572	2,696
Finance lease liabilities, current portion	689	681
Other current liabilities	106	—
Total current liabilities	\$ 110,617	\$ 34,570
Non-current liabilities		
Deferred revenue, net of current portion	77,838	29,642
Operating lease liabilities, net of current portion	14,128	16,651
Finance lease liabilities, net of current portion	604	1,165
Other non-current liabilities	100	—
Total liabilities	\$ 203,287	\$ 82,028
Commitments and contingencies (Note 9)		
Series Seed Convertible Preferred Stock, \$0.0001 par value; 0 and 3,000,000 shares authorized, issued and outstanding at December 31, 2020 and December 31, 2019, respectively (liquidation preference of \$3,000 at December 31, 2019)	\$ —	\$ 5,900
Series A Convertible Preferred Stock, \$0.0001 par value; 0 and 14,886,305 shares authorized and issued at December 31, 2020 and December 31, 2019, respectively and 0 and 14,720,126 shares outstanding at December 31, 2020 and December 31, 2019, respectively (liquidation preference of \$29,440 at December 31, 2019)	—	29,237
Series B Convertible Preferred Stock, \$0.0001 par value; 0 and 16,009,848 shares authorized at December 31, 2020 and December 31, 2019, respectively and 0 and 14,827,580 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively (liquidation preference of \$60,200 at December 31, 2019)	—	59,918
Series B-1 Convertible Preferred Stock, \$0.0001 par value; 0 and 3,059,695 shares authorized, issued and outstanding at December 31, 2020 and December 31, 2019, respectively (liquidation preference of \$20,000 at December 31, 2019)	—	14,025
Stockholders' equity (deficit):		
Preferred stock, \$0.0001 par value; 10,000,000 and 0 shares authorized as of December 31, 2020 and December 31, 2019, respectively; 0 shares issued or outstanding as of December 31, 2020 and December 31, 2019	—	—
Common stock, \$0.0001 par value; 150,000,000 and 45,000,000 shares authorized at December 31, 2020 and December 31, 2019, respectively, 44,592,288 and 2,208,982 shares issued at December 31, 2020 and December 31, 2019, respectively; 44,482,186 and 1,929,516 shares outstanding at December 31, 2020 and December 31, 2019, respectively	4	—
Additional paid-in capital	412,777	2,044
Accumulated deficit	(128,765)	(76,456)
Accumulated other comprehensive (loss) income	(128)	6
Total stockholders' equity (deficit)	283,888	(74,406)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	\$ 487,175	\$ 116,702

The accompanying notes are an integral part of these consolidated financial statements.

KYMERA THERAPEUTICS, INC.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year ended December 31,	
	2020	2019
Statement of Operations Data:		
Collaboration Revenue—from related party	\$ 34,034	\$ 2,934
Operating expenses:		
Research and development	\$ 62,105	\$ 37,158
General and administrative	18,233	7,981
Total operating expenses	80,338	45,139
Loss from operations	(46,304)	(42,205)
Other income (expense):		
Interest Income	826	1,005
Interest Expense	(115)	(46)
Total other income	711	959
Net loss	\$ (45,593)	\$ (41,246)
Other comprehensive loss:		
Unrealized (loss) gain on marketable securities	(134)	6
Total comprehensive loss	\$ (45,727)	\$ (41,240)
Reconciliation of net loss to net loss attributable to common stockholders:		
Net Loss	\$ (45,593)	\$ (41,246)
Deemed dividend from exchange of convertible preferred stock	(9,050)	—
Net loss attributable to common stockholders	\$ (54,643)	\$ (41,246)
Net loss per share attributable to common stockholders, basic and diluted	\$ (3.15)	\$ (24.28)
Weighted average common stocks outstanding, basic and diluted	17,349,582	1,698,522

The accompanying notes are an integral part of these consolidated financial statements.

KYMERA THERAPEUTICS, INC.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share and per share amounts)

	Series Seed Convertible Preferred Stock		Series A Convertible Preferred Stock		Series B Convertible Preferred Stock	
	Shares	Value	Shares	Value	Shares	Value
Balance at December 31, 2018	3,000,000	\$ 5,900	14,498,547	\$ 28,794	9,605,905	\$ 38,735
Vesting of Series A Preferred Stock in connection with collaboration arrangement (Note 5)	—	—	221,579	443	—	—
Issuance of Series B Convertible Preferred Stock, net of issuance costs of \$17	—	—	—	—	5,221,675	21,183
Issuance of Series B-1 Preferred Stock, net of issuance costs of \$49	—	—	—	—	—	—
Exercise of Stock Options	—	—	—	—	—	—
Vesting Restricted Stock	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—
Unrealized gain on marketable securities	—	—	—	—	—	—
Net Loss	—	—	—	—	—	—
Balance at December 31, 2019	3,000,000	\$ 5,900	14,720,126	\$ 29,237	14,827,580	\$ 59,918
Vesting of Series A Preferred Stock in connection with collaboration arrangement (Note 5)	—	—	110,788	222	—	—
Issuance of Series B Preferred Stock, net of issuance costs of \$0	—	—	—	—	1,182,265	4,800
Issuance of Series C Preferred Stock, net of issuance costs of \$320	—	—	—	—	—	—
Exchange of Series A Convertible Preferred Stock for Series C Preferred Convertible Preferred Stock	—	—	(1,988,802)	(3,950)	—	—
Exercise of Stock Options	—	—	—	—	—	—
Vesting Restricted Stock	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—
Unrealized loss on marketable securities	—	—	—	—	—	—
Issuance of shares in connection with initial public offering net of underwriting discounts and offering costs of \$17,003	—	—	—	—	—	—
Conversion of convertible preferred stock into common stock	(3,000,000)	(5,900)	(12,842,112)	(25,509)	(16,009,845)	(64,718)
Issuance of shares in concurrent private placement	—	—	—	—	—	—
Net Loss	—	—	—	—	—	—
Balance at December 31, 2020	—	\$ —	—	\$ —	—	\$ —

The accompanying notes are an integral part of these consolidated financial statements.

	Series B-1 Convertible Preferred Stock		Series C Convertible Preferred Stock		Common Stock		Additional Paid in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Consolidated Members' and Stockholders' Equity (Deficit)
	Shares	Value	Shares	Value	Shares	Value				
	—	\$ —	—	\$ —	1,479,188	\$ —				
Balance at December 31, 2018	—	\$ —	—	\$ —	1,479,188	\$ —	\$ 774	\$ (35,210)	\$ —	\$ (34,436)
Vesting of Series A Preferred Stock in connection with collaboration arrangement (Note 5)	—	—	—	—	—	—	—	—	—	—
Issuance of Series B Convertible Preferred Stock, net of issuance costs of \$17	—	—	—	—	—	—	—	—	—	—
Issuance of Series B-1 Preferred Stock, net of issuance costs of \$49	3,059,695	14,025	—	—	—	—	—	—	—	—
Exercise of Stock Options	—	—	—	—	95,904	—	74	—	—	74
Vesting Restricted Stock	—	—	—	—	354,424	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	1,196	—	—	1,196
Unrealized gain on marketable securities	—	—	—	—	—	—	—	6	—	6
Net Loss	—	—	—	—	—	—	—	(41,246)	—	(41,246)
Balance at December 31, 2019	3,059,695	\$ 14,025	—	\$ —	1,929,516	\$ —	\$ 2,044	\$ (76,456)	\$ 6	\$ (74,406)
Vesting of Series A Preferred Stock in connection with collaboration arrangement (Note 5)	—	—	—	—	—	—	—	—	—	—
Issuance of Series B Preferred Stock, net of issuance costs of \$0	—	—	—	—	—	—	—	—	—	—
Issuance of Series C Preferred Stock, net of issuance costs of \$320	—	—	13,539,141	88,180	—	—	—	—	—	—
Exchange of Series A Convertible Preferred Stock for Series C Preferred Convertible Preferred Stock	—	—	1,988,802	13,000	—	—	(2,334)	(6,716)	—	(9,050)
Exercise of Stock Options	—	—	—	—	78,852	—	162	—	—	162
Vesting Restricted Stock	—	—	—	—	184,410	—	112	—	—	112
Stock-based compensation expense	—	—	—	—	—	—	5,190	—	—	5,190
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	(134)	(134)
Issuance of shares in connection with initial public offering net of underwriting discounts and offering costs of \$17,003	—	—	—	—	9,987,520	1	182,747	—	—	182,748
Conversion of convertible preferred stock into common stock	(3,059,695)	(14,025)	(15,527,943)	(101,180)	31,625,534	3	211,329	—	—	211,332
Issuance of shares in concurrent private placement	—	—	—	—	676,354	—	13,527	—	—	13,527
Net Loss	—	—	—	—	—	—	—	(45,593)	—	(45,593)
Balance at December 31, 2020	—	\$ —	—	\$ —	44,482,186	\$ 4	\$ 412,777	\$ (128,765)	\$ (128)	\$ 283,888

(Continued from previous page)

The accompanying notes are an integral part of these consolidated financial statements.

KYMERA THERAPEUTICS, INC.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2020	2019
Operating activities		
Net loss	\$ (45,593)	\$ (41,246)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	5,190	1,196
Depreciation and amortization	1,763	825
Non-cash research and development expense	332	443
Net amortization of premiums and discounts on investments	1,571	—
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(3,816)	(564)
Accounts receivable—due from related party	(577)	—
Contract asset—due from related parties	(856)	—
Other receivables—due from related parties	—	148
Accounts payable	990	904
Accrued expenses and other current liabilities	5,754	2,248
Deferred revenue	117,400	52,991
Other non-current assets	(30)	—
Operating lease right-of-use assets	8,444	1,350
Operating lease liabilities	(2,647)	(383)
Other non-current liabilities	205	(7)
Net cash provided by operating activities	\$ 88,130	\$ 17,905
Investing activities		
Purchase of property and equipment, net	(9,096)	(532)
Purchase of marketable securities	(529,382)	(15,954)
Maturities of marketable securities	115,890	—
Net cash used in investing activities	\$ (422,588)	\$ (16,486)
Financing activities		
Proceeds from the issuance of Series B Convertible Preferred Stock, net of issuance costs	—	21,183
Proceeds from the issuance of Series B-1 Convertible Preferred Stock, net of issuance costs	4,800	14,025
Proceeds from the issuance of Series C Convertible Preferred Stock, net of issuance costs	88,181	—
Proceeds from stock option exercises	162	74
Payments on financing leases	(554)	(371)
Proceeds from initial public offering, net of underwriting discounts and offering costs	183,146	—
Proceeds from concurrent private placement	13,527	—
Net cash provided by financing activities	\$ 289,262	\$ 34,911
Net (decrease) increase in cash, cash equivalents and restricted cash	(45,196)	36,330
Cash, cash equivalents and restricted cash at beginning of period	77,789	41,459
Cash, cash equivalents and restricted cash at end of period	\$ 32,593	\$ 77,789
Supplemental disclosure of cash flow activities		
Cash paid for interest	\$ 115	\$ 46
Supplemental disclosure of noncash investing and financing activities		
Purchases of property and equipment through finance and lease liabilities	\$ —	\$ 1,642
Property and equipment purchases included in accounts payable and accrued expenses	\$ 27	\$ 315
Offering costs included in accounts payable	\$ 397	\$ —
Supplemental disclosure of noncash operating activities		
Right-of-use assets obtained in exchange for operating lease liabilities	\$ —	\$ 16,522
Tenant improvement receivable included in other assets	\$ —	\$ 287
Reduction of right-of-use asset and liability due to lease modification	\$ 2,161	\$ —

The accompanying notes are an integral part of these consolidated financial statements.

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the periods shown above:

	December 31,	
	2020	2019
Cash and cash equivalents	\$ 31,004	\$ 76,015
Restricted cash	1,589	1,774
Total cash, cash equivalents, and restricted cash	<u>\$ 32,593</u>	<u>\$ 77,789</u>

KYMERA THERAPEUTICS, INC
Notes to Consolidated Financial Statements

Note 1. Description of Business and Summary of Significant Accounting Policies

Kymera Therapeutics, Inc., together with its subsidiary Kymera Securities Corporation, is referred to on a consolidated basis as the “Company”. The Company is a biopharmaceutical company focused on discovering and developing small molecule therapeutics that selectively degrade disease-causing proteins by harnessing the body’s own natural cellular process, a method known as targeted protein degradation. The Company has devoted its efforts principally to research and development since formation. The Company has not yet completed product development, filed for or obtained regulatory approvals for any products, nor verified the market acceptance and demand for such products. As a result, the Company is subject to a number of risks common to emerging companies in the biotech industry. Principal among these risks are the uncertainties of the product discovery and development process, dependence on key individuals, development of the same or similar technological innovations by the Company’s competitors, protection of proprietary technology, compliance with government regulations and approval requirements, the Company’s ability to access capital and uncertainty of market acceptance of products.

The Company has historical net losses and anticipates that it will continue to incur losses for the foreseeable future and had an accumulated deficit of \$128.8 million as of December 31, 2020. The Company has funded these losses principally through issuance common stock, including its initial public offering (“IPO”), which was completed in August 2020, preferred stock, convertible notes and from cash proceeds received in connection with the Company’s collaboration agreements with Vertex Pharmaceuticals Incorporated (“Vertex”) and Genzyme Corporation (“Sanofi”) (see Note 5). The Company expects to continue to incur operating losses and negative cash flows until such time as it generates a level of revenue that is sufficient to support its cost structure.

As of December 31, 2020, the Company had cash, cash equivalents and marketable securities of \$458.7 million. The Company believes these cash, cash equivalents and marketable securities will be sufficient to fund its operations and capital expenditure requirements through at least twelve months from the issuance of these consolidated financial statements.

The Company expects to finance the future research and development costs of its product portfolio with its existing cash, cash equivalents and marketable securities, or through strategic financing opportunities that could include, but are not limited to future offerings of its equity, collaboration agreements, or the incurrence of debt. However, there is no guarantee that any of these strategic or financing opportunities will be executed or realized on favorable terms, if at all, and some could be dilutive to existing stockholders. If the Company fails to obtain additional future capital, it may be unable to complete its planned preclinical studies and clinical trials.

Reverse Stock Split

On August 20, 2020, the Board approved a 1-for-1.5949 reverse stock split of the Company’s issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each of the Company’s outstanding series of preferred stock. All share and per share amounts in the accompanying consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

Initial Public Offering

On August 20, 2020, the Company’s registration statement on Form S-1 relating to its initial public offering of its common stock was declared effective by the Securities and Exchange Commission (“SEC”). In the IPO, which closed on August 25, 2020, the Company issued and sold 9,987,520 shares of common stock, including full exercise of the underwriters’ over-allotment option to purchase an additional 1,302,720 shares, at a public offering price of \$20.00 per share and the aggregate gross proceeds before deducting before deducting underwriting discounts and commissions, and other estimated offering expenses payable by the Company, were approximately \$199.8 million. Concurrent with the IPO, the Company issued and sold 676,354 shares of common stock at \$20.00 per share in a private placement to Vertex.

Note 2. Summary of Significant Accounting Policies

The accompanying consolidated financial statements reflect the application of certain significant accounting policies as described in this note, and elsewhere in the accompanying consolidated financial statements and notes.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary Kymera Securities Corporation. All intercompany transactions and balances have been eliminated in consolidation.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and judgments that affect the reported amounts of assets and liabilities and disclosure of contingencies at the date of the financial statements and the reported amounts of expenses during the reporting period. Management's estimates and judgments are derived and continually evaluated based on available information, historical experience and various other assumptions that are believed to be reasonable under the circumstances. Because the use of estimates is inherent in the financial reporting process, actual results could differ from those estimates. In recording transactions and balances resulting from business operations, management makes estimates based on the best information available at the time the estimate is made. Significant estimates relied upon in preparing these financial statements include revenue recognized under our collaboration agreement with Sanofi and Vertex, accrual for research and development expenses, equity-based compensation expense, and the valuation of equity. As better information becomes available or actual amounts are determinable, the recorded estimates are revised. Consequently, operating results can be affected by revisions to prior estimates.

Segment and Geographic Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company's chief operating decision maker is the Chief Executive Officer. The Company views its operations and manages its business in one operating segment.

Cash and Cash Equivalents

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. These assets include investments in money market funds that invest in U.S. Treasury obligations and corporate bonds. The Company maintains its bank accounts at major financial institutions.

Restricted Cash

Restricted cash represents the cash held to secure a letter of credit associated with the Company's facility lease.

Marketable Securities

The Company classifies marketable securities with a remaining maturity of greater than three months when purchased as available-for-sale. The Company classifies investments available to fund current operations as current assets on its balance sheets. Marketable securities with a remaining maturity date greater than one year are classified as non-current. Available-for-sale securities are maintained by investment managers and consist of U.S. Treasury securities and corporate bonds. Available-for-sale securities are carried at fair value with the unrealized gains and losses included in other comprehensive income (loss) as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other (expense) income, net.

If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other-than-temporary" and, if so, marks the investment to market through a charge to the Company's statement of operations and comprehensive loss.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

Level 1—Quoted prices in active markets for identical assets

Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar asset, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets, including pricing models, discounted cash flow methodologies and similar techniques.

The carrying values of the Company's cash equivalents, prepaid expenses, accounts payable, and certain accruals approximate their fair value due to their short-term nature.

Leases

The Company adopted ASC Topic 842, *Leases* ("ASC 842") on January 1, 2019. At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present. Leases that are economically similar to the purchase of assets are generally classified as finance leases; otherwise the leases are classified as operating leases. The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets, lease liabilities and, if applicable, long-term lease liabilities. Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. However, certain adjustments to the right-of-use asset may be required for items such as incentives received. The Company has elected as an accounting policy to combine lease and non- lease components, such as common area maintenance, for all classes of underlying assets. The interest rate implicit in lease contracts has not historically been readily determinable. As a result, the Company utilizes its incremental borrowing rates, which are the rates incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. To estimate its incremental borrowing rate, a credit rating applicable to the Company is estimated using synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating.

Property and Equipment

Property and equipment are recorded at cost, net of accumulated depreciation. Major additions and betterments are capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to operations as incurred. Depreciation expense is recorded using the straight-line method over the estimated useful life of the related asset as follows:

	Estimated Useful Life (in years)
Lab equipment	5 years
Furnitures and fixtures	5 years
Office equipment	5 years
Computer equipment	3 years
Leasehold improvements	Shorter of life of lease or remaining lease term

Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is included in loss from operations.

Construction-in-progress is stated at cost, which includes direct costs attributable to the setup or construction of the related asset. Depreciation expense is not recorded on construction-in-progress until the relevant assets are completed and put into use.

Impairment of Long-Lived Assets

Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2020 and 2019.

Convertible Preferred Stock

The Company classified convertible preferred stock as temporary equity in the accompanying consolidated balance sheet due to terms that allow for redemption of the shares in cash upon certain change in control events that are outside of the Company's control, including the sale or transfer of the Company as holders of the convertible preferred stock which could trigger redemption of the shares. The Company did not accrete the value of the convertible preferred stock to the redemption values since a liquidation event was not considered probable as of December 31, 2019. Subsequent adjustments of the carrying values to the ultimate redemption values will be made only when it becomes probable that such liquidation events will occur. In connection with the Company's initial public offering on August 21, 2020, all outstanding shares of convertible preferred stock converted to common stock.

Research and Development Costs

Research and development costs consist primarily of costs incurred in connection with the discovery and development of targeted protein degradation therapeutics, including those in the Company's most advanced development programs, IRAK4, IRAKIMiD and STAT3. These research efforts and costs, which also support the development of, and enhancements to, the Company's Pegasus targeted protein degradation platform, include external research costs, personnel costs, supplies, license fees and facility related expenses. The Company expenses research and development costs as incurred.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recoverability of the expenditure. Amounts incurred are classified as general and administrative expenses.

Financing Costs

Costs incurred in connection with the issuance of equity units and shares are recorded as a reduction of proceeds to the equity carrying value. The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process financings as deferred offering costs until such financings are consummated. After consummation of the financing, these costs are recorded as a reduction of the proceeds received from the financing. If a planned financing is abandoned, the deferred offering costs are expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. There was \$0.4 million of deferred financing costs included in accounts payable on the Company's consolidated balance sheet as of December 31, 2020. There was no deferred offering costs on the Company's consolidated balance sheet at December 31, 2019.

Revenue Recognition

The Company adopted ASC Topic 606, *Revenue from Contracts with Customers* (“ASC 606”) on January 1, 2017. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the contract(s) with the customer; (ii) identification of the promised goods or services in the contract and determination of whether the promised goods or services are performance obligations; (iii) measurement of the transaction price; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above and whether those performance obligations are distinct from other performance obligations in the contract; b) the transaction price under step (iii) above; and c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. In determining the stand-alone selling price of a license to the Company’s proprietary technology or a material right provided by a customer option, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed estimates that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating its estimated stand-alone selling prices, the Company evaluates whether changes in the key assumptions used to determine its estimated stand-alone selling prices will have a significant effect on the allocation of arrangement consideration between performance obligations.

The Company estimates the transaction price based on the amount of consideration the Company expects to be received for transferring the promised goods or services in the contract. The consideration may include both fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of the potential payments and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected value method to estimate the transaction price based on which method better predicts the amount of consideration expected to be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price.

Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when: (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own and whether the required expertise is readily available.

For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation in order to determine whether the combined performance obligation is satisfied over time or at a point in time. The Company receives payments from customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. Amounts are recorded as accounts receivable when the Company’s right to consideration is unconditional. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

Exclusive Licenses—If the license granted in the arrangement is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, the Company considers relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promise, whether the value of the license is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the arrangement.

Research and Development Services—The promises under the Company’s collaboration and license agreements generally include research and development services to be performed by the Company on behalf of the collaboration partner. For performance obligations that include research and development services, the Company generally recognizes revenue allocated to such performance obligations based on an appropriate measure of progress. The Company utilizes judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure, such as costs incurred. The Company evaluates the measure of progress each reporting period as described under Exclusive Licenses above. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are generally recorded as a reduction to research and development expense.

Customer Options—The Company’s arrangements may provide a collaborator with the right to certain optional purchases, such as the right to license a target either at the inception of the arrangement or within a pre-defined option period. Under these agreements, fees may be due to the Company at the inception of the arrangement as an upfront fee or payment or upon the exercise of an option to acquire a license. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. The Company allocates the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount, and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments—At the inception of each arrangement that includes milestone payments based on certain events, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to the Company’s efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Royalties—For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Collaboration revenue—The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808, *Collaborative Arrangements* (“ASC 808”) to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to Topic 606. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above.

Costs associated with License and Collaborative Arrangements

Costs associated with licenses of technology acquired as part of collaborative arrangements are expensed as incurred and are generally included in research and development expense in the consolidated statements of operations.

Stock-Based Compensation

The Company accounts for all stock-based awards granted to employees, directors, and nonemployees based on their fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. Stock-based payments include stock options and grants of common stock, including common stock subject to vesting. The measurement date for stock awards is the date of grant, and stock-based compensation costs are recognized as expense over the requisite service period, which is the vesting period, on a straight-line basis. The Company has issued stock options and restricted stock with performance-based vesting conditions and records the expense for these awards if the Company concludes that it is probable that the performance condition will be achieved. Stock-based compensation is classified in the accompanying consolidated statements of operations and comprehensive loss based on the function to which the related services are provided. The Company recognizes stock-based compensation expense for the portion of awards that have vested. Forfeitures are accounted for as they occur.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes options-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and the Company’s expected dividend yield. Prior to the IPO, as there was no active market for the Company’s common stock, the Company estimated the fair value of common stock on the date of grant based on the then current facts and circumstances. Upon becoming a public company, the fair value of the underlying common shares equals the closing price of the Company’s stock on the date of grant. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of guideline companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company’s stock options has been determined utilizing the “simplified” method for awards that qualify as “plain-vanilla” options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of the Company’s common stock on that same date.

Compensation expense for discounted purchases under the employee stock purchase plan is measured using the Black-Scholes model to compute the fair value of the lookback provision plus the purchase discount and is recognized as compensation expense over the offering period.

Common and Preferred Stock Valuation

The Company utilized significant estimates and assumptions in determining the fair value of its equity and equity-based awards. The Company utilized various valuation methodologies in accordance with the framework of the 2013 American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its equity awards.

The Company used a hybrid of the probability-weighted expected returns method (“PWERM”), and the option pricing method (“OPM”) when allocating enterprise value to classes of securities.

Under the probability-weighted expected return method, or PWERM, the value of an enterprise, and its underlying common securities, are estimated based on an analysis of future values for the enterprise, assuming various outcomes. The value of the common securities is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes and the rights of each class of equity. The future values of the common securities under the various outcomes are discounted back to the valuation date at an appropriate risk-adjusted discount rate and then probability weighted to determine the value for the common securities.

The option pricing method, or OPM, treats common securities and preferred securities as call options on the enterprise's equity value, with exercise prices based on the liquidation preferences of the preferred securities. Under this method, the common securities have value only if the funds available for distribution to shareholders exceed the value of the liquidation preferences at the time of a liquidity event. The Black-Scholes model is used to price the call option, and the model includes assumptions for the time to liquidity and the volatility of equity value.

The hybrid method is a hybrid between the PWERM and OPM, estimating the probability-weighted value across multiple scenarios but using the OPM to estimate the allocation of value within one or more of those scenarios.

Valuations performed in the year ended December 31, 2020 and 2019, used a hybrid of the PWERM and OPM when allocating the Company's enterprise value to classes of securities.

When using the hybrid method, the Company assumed two scenarios: an IPO scenario and a trade-sale scenario. The IPO scenario estimated an equity value based on the guideline public company method under a market approach. The guideline public companies considered for this scenario consist of biopharmaceutical companies with recently completed initial public offerings. The Company converted its estimated future value in an IPO to present value using a risk-adjusted discount rate. The equity value for the trade-sale scenario was estimated using the price of a recently issued preferred security, as well as a milestone-based tranche closing. The Company utilized an option pricing model to quantify or attribute value to these economic rights of convertible preferred stock vs. the common stock (e.g. liquidation preferences, dividend provisions, participation rights after liquidation preferences.)

In the OPM, volatility is estimated based on the trading histories of selected guideline public companies. The relative probability of each scenario was determined based on an assessment of then-current market conditions and the Company's expectations as to timing and prospects of an IPO.

Each valuation methodology includes estimates and assumptions that require significant judgment. These estimates and assumptions include a number of objective and subjective factors, including the prices at which shares were traded between holders of the Company, external market conditions, the prices at which the Company sold convertible preferred shares, the superior rights and preferences of securities senior to common shares at the time, and the likelihood of achieving a voluntary or involuntary liquidity event.

Significant changes to the key assumptions used in the valuations could result in different fair values of common shares at each valuation date, as applicable.

Income Taxes

Income taxes for Kymera Therapeutics, Inc. are recorded in accordance with FASB Accounting Standards Codification Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred income tax assets and liabilities are recognized based on future income tax consequences attributable to differences between the financial statement carrying amount of existing assets and liabilities, and their respective income tax basis. Deferred income tax assets and liabilities are measured using enacted income tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of changes in income tax rates on deferred income tax assets and liabilities is recognized as income or expense in the period that a valuation allowance for any income tax benefits of which future realization is not more likely than not.

The Company provides reserves for potential payments of tax to various tax authorities related to uncertain tax positions. The tax benefits recorded are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is "more likely than not" to be realized following resolution of any uncertainty related to the tax benefit, assuming that the matter in question will be raised by the tax authorities.

Off Balance Sheet Risk and Concentration of Credit Risk

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, and restricted cash. The Company's cash, cash equivalents, and restricted cash are deposited in accounts at large financial institutions. The Company believes it is not exposed to significant credit risk due to the financial strength of the depository institutions in which the cash, cash equivalents and restricted cash are held. The Company maintains its cash equivalents in money market funds that invest in U.S. Treasury securities and U.S. Treasury obligations and corporate bonds. The Company's marketable securities primarily consist of corporate bonds and U.S. Treasury securities paper, and potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy that limits the amounts the Company may invest in any one type of investment. The Company has not experienced any credit losses and does not believe it is exposed to any significant credit risk on these funds.

Comprehensive Loss

Comprehensive loss includes net loss as well as unrealized gains on marketable securities and other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders.

Net Loss Per Share

The Company applies the two-class method to compute basic and diluted net income (loss) per share attributable to common stockholders when it has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (loss) available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to share in the earnings as if all income (loss) for the period had been distributed. The Company's convertible preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. The participating securities are not required to participate in the losses of the Company, and therefore during periods of loss there is no allocation required under the two-class method.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) attributable to common stockholders is computed by adjusting net income (loss) per share attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period, including potential dilutive common shares. For purpose of this calculation, outstanding options to purchase common stock, unvested restricted stock awards, and shares of convertible preferred stock are considered potential dilutive common shares. The Company has generated a net loss in all periods presented, and therefore the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive.

Emerging Growth Company Status

The Company is an emerging growth company ("EGC"), as defined in the Jumpstart Our Business Startups Act (the "JOBS Act"), and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act, which provides that an EGC can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use this exemption to delay adopting new or revised.

Recent Accounting Pronouncements

Recently Adopted Accounting Standards

In April 2019, the FASB issued ASU 2019-04, *Codification Improvements to Topic 326, Financial Instruments—Credit Losses, Topic 815, Derivatives and Hedging, and Topic 825, Financial Instruments*. This update provides clarifications for three topics related to financial instruments accounting, some of which apply to the Company. The Company adopted as of January 1, 2020 and it did not have a significant impact on its financial position or results of operation

In August 2018, the FASB issued ASU 2018-15, *Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*. The new standard will align the requirements for capitalizing implementation costs for hosting arrangements (services) with costs for internal-use software (assets). As a result, certain implementation costs incurred in hosting arrangements will be deferred and amortized. The Company adopted as of January 1, 2020 and it did not have a significant impact on its financial position or results of operation.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*. The new standard will be effective beginning January 1, 2020. The Company adopted as of January 1, 2020 and it did not have a significant impact on its financial position or results of operation.

Recently Issued Accounting Standards Not Yet Adopted

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard will be effective beginning January 1, 2021. The Company is currently evaluating the potential impact ASU 2019-12 may have on its financial position and results of operations upon adoption.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Statements*. The new standard requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. It also limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and also requires the reversal of previously recognized credit losses if fair value increases. As an emerging growth company, the Company expects to delay adoption until January 1, 2023 and is evaluating the impact that the adoption of ASU 2016-13 will have on its consolidated financial statements.

Note 3. Fair Value Measurements

The following table presents information about the Company's financial assets measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values as of December 31, 2020 and December 31, 2019 (in thousands):

	Fair Value Measurements at December 31, 2020:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents				
Money market fund	\$ 19,943	\$ —	\$ —	\$ 19,943
Corporate bonds	—	10,499	—	10,499
Marketable securities, current				
US treasuries	192,275	—	—	192,275
Corporate bonds	—	72,923	—	72,923
Marketable securities, non-current				
US treasuries	132,589	—	—	132,589
Corporate bonds	—	29,942	—	29,942
Restricted cash	1,589	—	—	1,589
Total	<u>\$ 346,396</u>	<u>\$ 113,364</u>	<u>\$ —</u>	<u>\$ 459,760</u>
	Fair Value Measurements at December 31, 2019:			
	Level 1	Level 2	Level 3	Total
Assets:				
Marketable securities				
Marketable securities	\$ 15,942	\$ —	\$ —	\$ 15,942
Restricted cash	1,774	—	—	1,774
Total	<u>\$ 17,716</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 17,716</u>

During the years ended December 31, 2020 and 2019, there were no transfers between Level 1, Level 2 and Level 3.

Note 4. Marketable Securities

The following table summarizes the available-for-sale debt securities held at December 31, 2020 and 2019 and (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
December 31, 2020				
U.S. treasury securities	\$ 324,917	\$ —	\$ (53)	\$ 324,864
Corporate securities	102,946	—	(81)	102,865
Total	<u>\$ 427,863</u>	<u>\$ —</u>	<u>\$ (134)</u>	<u>\$ 427,729</u>
December 31, 2019				
U.S. treasury securities	\$ 15,936	\$ 6	\$ —	\$ 15,942
Total	<u>\$ 15,936</u>	<u>\$ 6</u>	<u>\$ —</u>	<u>\$ 15,942</u>

As of December 31, 2020, the Company held 65 securities that had been in an unrealized loss position for less than 12 months with an aggregate fair value of \$392.2 million. As of December 31, 2019, the Company did not hold any securities that were in an unrealized loss position.

As of December 31, 2020, the Company had 48 securities with a fair value of \$295.6 million with a contractual maturity of less than 12 months and 25 securities with a fair value of \$162.5 million with a contractual maturity of greater than 12 months. As of December 31, 2019, all of the Company's marketable securities had remaining contractual maturity dates of less than one year from the consolidated balance sheet date. During the year ending December 31, 2020, the Company sold one security prior maturity which resulted in an immaterial realized gain on the sale. There were no sales of marketable securities during the year ended December 31, 2019.

The Company evaluates securities for other-than-temporary impairments based on quantitative and qualitative factors, and considered the decline in market value for the 65 securities in an unrealized loss position as of December 31, 2020, to be primarily attributable to the then current economic and market conditions. The Company neither intends to sell these investments nor concludes that it is more-likely-than-not that the Company will have to sell them before recovery of their carrying values. The Company also believe that it will be able to collect both principal and interest amounts due to it at maturity.

Note 5. Collaborations

Sanofi Collaboration Arrangement

Agreement Terms

On July 7, 2020, the Company entered into a collaboration agreement, or the Sanofi Agreement, with Sanofi, to co-develop drug candidates directed to two biological targets. Under the Sanofi Agreement, the Company granted to Sanofi a worldwide exclusive license to develop, manufacture and commercialize certain lead compounds generated during the collaboration directed against IRAK4, or Collaboration Target 1, and one additional undisclosed target in an undisclosed field of use, or Collaboration Target 2. Such license is exercisable on a collaboration target-by-collaboration target basis only after specified milestones. For compounds directed against IRAK4, the field of use includes diagnosis, treatment, cure, mitigation or prevention of any diseases, disorders or conditions, excluding oncology and immune-oncology.

Pursuant to the Sanofi Agreement, the Company is responsible for discovery and preclinical research and conducting a Phase 1 clinical trial for at least one degrader directed against IRAK4 plus up to three backup degraders. With respect to both targets, Sanofi is responsible for development, manufacturing, and commercialization of product candidates after a specified development milestone occurs with respect to each collaboration candidate.

In addition, pursuant to the Sanofi Agreement, Sanofi will grant to the Company an exclusive option, or Opt-In Right, exercisable on a collaboration target-by-collaboration target basis that will include the right to (i) to fund 50% of the United States development costs for collaboration products directed against such target in the applicable field of use and (ii) share equally in the net profits and net losses of commercializing collaboration products directed against such target in the applicable field of use in the United States. In addition, if the Company exercises the Opt-In Right, Sanofi will grant to the Company an exclusive option, applicable to each collaboration target, which upon exercise will allow the Company to conduct certain co-promotion activities in the field in the United States.

The Sanofi Agreement, unless earlier terminated, will expire on a product-by-product basis on the date of expiration of all payment obligations under the Sanofi Agreement with respect to such product. The Company or Sanofi may terminate the agreement upon the other party's material breach or insolvency or for certain patent challenges. In addition, Sanofi may terminate the agreement for convenience or for a material safety event upon advance prior written notice, and the Company may terminate the agreement with respect to any collaboration candidate if, following Sanofi's assumption of responsibility for the development, commercialization or manufacturing of collaboration candidates with respect to a particular target, Sanofi ceases to exploit any collaboration candidates directed to such target for a specified period.

In consideration for the exclusive licenses granted to Sanofi under the Sanofi Agreement, Sanofi paid to the Company an upfront payment of \$150.0 million. The Company will also be reimbursed for certain research activities for a certain backup degrader under the IRAK4 program, unless certain criteria are not met for an initial IRAK4 degrader. In addition to the upfront payment and the reimbursements, the Company is eligible to receive certain development milestone payments of up to \$1.48 billion in the aggregate, of which more than \$1.0 billion relates to the IRAK4 program, upon the achievement of certain developmental or regulatory events. The Company will be eligible to receive certain commercial milestone payments up to \$700.0 million in the aggregate, of which \$400 million relates to the IRAK4 program, which are payable upon the achievement of certain net sales thresholds. The Company will be eligible to receive tiered royalties for each program on net sales ranging from the high single digits to high teens, subject to low-single digits upward adjustments in certain circumstances.

Accounting Treatment

The Company analyzed the discovery and pre-clinical research activities as well as the exclusive license grants under the Sanofi Agreement and concluded that the arrangement was indicative of a vendor-customer relationship and would be accounted for under ASC 606.

The Company identified the following material promises under the arrangement: (1) research services for Collaboration Target 1, (2) research license for Collaboration Target 1, (3) exclusive license for Collaboration Target 1, (4) research services for Collaboration Target 2, (5) research license for Collaboration Target 2, (6) exclusive license for Collaboration Target 2, (7) option to extend the research term, and (8) optional research services during the development period.

The Company determined that Collaboration Targets 1 and 2 are distinct from each other. The research associated with degraders directed to each target is at different stages and the licensed field, should development activities be successful, are different from each other. As such, all promises associated with each target are considered distinct from promises associated with the other target.

The research and development services for each collaboration target were determined not to be distinct from the research license and the exclusive license and have been combined into a single performance obligation for each collaboration target. That is, two performance obligations were identified, the combined research services, research license and exclusive license for Collaboration Target 1 and the combined research services, research license and exclusive license for Collaboration Target 2. The exclusive license for each target is not distinct from the pre-clinical and clinical research and development services under the Sanofi Agreement, primarily due to the highly specialized nature of the research and novel technology involved with developing protein degraders – the pre-clinical activities and studies and first phase 1 clinical trial could not be conducted by another party in the manner required.

The option to extend the research term and optional research services during the development period were evaluated as material rights. The fees associated with each option are at or above the standalone selling price. As such, the underlying options are not performance obligations and fees associated with each option are excluded from the transaction price until the underlying option is exercised.

The Company determined the total transaction price to be \$150.0 million, which consists solely of the upfront payment. All milestones payments and option payments are constrained as the achievement of such milestones are contingent upon the success of the underlying research and development activities and are generally outside the control of the Company. The reimbursement of costs for the IRAK4 backup degrader is also treated as constrained variable consideration as the criteria for reimbursement may not always be met, under which circumstances the Company would be responsible for the costs related to the backup degrader. Upon becoming unconstrained, the reimbursement consideration will be added to the transaction price and allocated to Collaboration Target 1.

The Company allocated the upfront payment to each performance obligation based on the relative standalone selling price, as follows:

- Collaboration Target 1: \$120.0 million
- Collaboration Target 2: \$30.0 million

The Company determined the allocation of the \$150.0 million transaction price between Collaboration Target 1 and Collaboration Target 2 based on the value of the research and development for the programs from projected research and development costs for each collaboration target plus a developer's profit and the total potential milestones for each collaboration target.

The Company recognizes revenue associated with each performance obligation as the research and development services are provided using an input method, according to costs incurred as related to the research and development activities for each individual program and the costs expected to be incurred in the future to satisfy that individual performance obligation. The transfer of control occurs over this time period and, in management's judgment, is the best measure of progress towards satisfying each performance obligation. The amounts received that have not yet been recognized as revenue are deferred as a contract liability on the Company's consolidated balance sheet and will be recognized over the remaining research and development period until the performance obligation is satisfied. Reimbursement consideration added to the transaction price will be recognized as revenue on the same pattern as Collaboration Target 1, with a cumulative catch-up upon becoming unconstrained. The performance obligation has not been fully satisfied as of December 31, 2020. During the year ended December 31, 2020, the Company recognized \$18.8 million in revenue under the Sanofi Agreement, of which \$16.7 million was associated with Collaboration Target 1 and \$2.1 million was associated with Collaboration Target 2. The aggregate amount of the transaction price allocated to the Company's unsatisfied performance obligations and recorded in deferred revenue at December 31, 2020 is \$132.6 million. As of December 31, 2020, the Company had not received cost reimbursement payments, and no milestone or royalty payments under the Sanofi Agreement. As of December 31, 2020, the Company recorded unbilled accounts receivable of \$0.9 million related to reimbursable research and development costs under the Sanofi Agreement for activities performed during the three months ended December 31, 2020 and \$0.6 million in accounts receivable for amounts billed under the Sanofi Agreement as of December 31, 2020. The Company will recognize the deferred revenue related to the performance obligations based on a cost input method, as described, over the remaining research term, which is a maximum of three years as of December 31, 2020.

Any consideration related to performance-based milestones will be recognized when the risk of probable reversal is resolved, at which point the Company shall adjust the transaction price determined for the agreement accordingly and recognize revenue on a cumulative-catch up basis, reallocating the revised arrangement consideration to the performance obligations. Any consideration related to sales milestone payments and royalties will be recognized when the related milestone events or sales occur and therefore are recognized at the later of when the related sales occur or the relevant performance obligation is satisfied. As part of its evaluation of constraining the milestones, the Company considered numerous factors, including the fact that the achievement of the research and development milestones are contingent upon the results of the underlying research and development activities and are thus outside of the control of the Company.

Sanofi participated in the Company's Series B Convertible Preferred Stock offering and as a result of this, is considered a related party.

Vertex Agreement

On May 9, 2019 (the "Effective Date"), the Company entered into a collaboration agreement (the "Vertex Agreement") with Vertex to advance small molecule protein degraders against up to six targets. Under the Vertex Agreement, Vertex has the exclusive option to license the rights to the product candidates developed for the designated targets at which point Vertex will control development and commercialization. Pursuant to the Vertex Agreement, the Company is only responsible for discovery and preclinical research on the targets, and Vertex is responsible for development, manufacturing, and commercialization of the product candidates after it exercises its option to license. The initial research term of the collaboration is four (4) years, extendable for an additional one (1) year period upon mutual agreement by the parties and payment by Vertex of certain per-target fees.

Vertex provided the Company with a non-refundable upfront payment of \$50.0 million and purchased 3,059,695 shares of the Company's Series B-1 Convertible Preferred Stock ("Series B-1") at \$6.54 a share, pursuant to a separate, but simultaneously executed Share Purchase Agreement. The shares were purchased at a premium of \$5.9 million, which was included in the transaction price and will be recognized as revenue over the period of performance. As a result of this purchase, Vertex is considered a related party.

The Company is eligible to receive up to \$170.0 million in payments per target, including development, regulatory and commercial milestones as well as option exercise payments. In addition, Vertex is obligated to pay the Company tiered royalties on future net sales on any products that may result from the Vertex Agreement. None of the payments under the Vertex Agreement are refundable. The Company may also perform follow-on research for an optioned target upon Vertex's request and at Vertex's expense.

The term of the Vertex Agreement began on the Effective Date and expires upon the expiration of all payment obligations from Vertex to Company under the Vertex Agreement or, if Vertex does not exercise any of its options, the lapse of all Vertex's option rights under the Vertex Agreement. Vertex also has the ability to terminate for convenience with prior written notice to the Company, and either party may terminate for an uncured material breach.

Accounting Treatment

The Company analyzed the joint research activities required under the Vertex Agreement and concluded that the arrangement was indicative of a vendor-customer relationship and would be accounted for under ASC 606.

The Company identified the following material promises under the arrangement: (1) the non-exclusive, royalty-free research license; and (2) the research and development services to be performed on up to six targets; and (3) the option to license each of the targets for development, manufacturing, and commercialization efforts. The research and development services were determined not to be distinct from the research and development license and have been combined into a single performance obligation. The Company determined that the option to license the targets in the future was not priced at a discount, and that the option exercise fee for each target is at or above the standalone selling price for research at this stage of development; as such, the options and the underlying licenses are excluded from the performance obligation and the option exercise fees are excluded from the transaction price until the underlying option is exercised.

As part of its evaluation of constraining the research and development milestones, the Company considered numerous factors, including the fact that the achievement of the research and development milestones are contingent upon the results of the underlying research and development activities and are thus outside of the control of the Company.

At the commencement of the arrangement, two units of accounting were identified, the issuance of 3,059,695 shares of the Company's Series B-1 Convertible Preferred Stock and the research activities the Company will perform over the Research Term. The Company determined the total transaction price to be \$55.9 million, which consists of \$5.9 million attributed to the premium from the Series B-1 shares sold to Vertex and the \$50.0 million upfront payment. To determine the fair value of the Series B-1 issued to Vertex, the Company performed a valuation of the shares of the Company's common and preferred stock, which took into consideration recent financings, and the Company's recent development and future exit strategies, as well as a discount for lack of marketability.

The Company recognizes revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities on each program and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs over this time period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation. The amounts received that have not yet been recognized as revenue are deferred as a contract liability on the Company's consolidated balance sheet and will be recognized over the remaining research and development period until the performance obligation is satisfied. The performance obligation has not been fully satisfied as of December 31, 2020. During the years ended December 31, 2020 and 2019, the Company recognized \$15.2 million and \$2.9 million in revenue under the Vertex Agreement. All \$15.2 million revenue recognized during the year ended December 31, 2020 was recognized from amounts that were recorded in deferred revenue as of December 31, 2019. The aggregate amount of the transaction price allocated to the Company's unsatisfied performance obligation and recorded in deferred revenue at December 31, 2020 and 2019 is \$37.7 million and \$53.0 million, respectively. The Company will recognize the deferred revenue related to the research and development services based on a cost input method, over the remaining research term, which is a maximum of 2.0 years as of December 31, 2020.

Any consideration related to sales milestone payments (including royalties) will be recognized when the related milestone events or sales occur and therefore are recognized at the later of when the related sales occur or the relevant performance obligation is satisfied.

Compound Collaboration

In October 2017, the Company entered into a collaboration agreement (the “Collaboration”) with a pharmaceutical company to jointly identify, research and conduct preclinical development of collaboration compounds against specified collaboration targets to identify drug candidates. Under the terms of the Collaboration, both parties provided one another with a non-exclusive, royalty-free, sub-licensable research and development license to each party’s intellectual property to develop five agreed-upon collaboration targets, as well as an exclusive, royalty-bearing development and commercialization license to sell any licensed products that stem from such research. The parties also have the ability to nominate additional collaboration targets if agreed-upon, as long as there are no more than five targets at any given time.

In exchange for the non-exclusive license rights, the Company provided the pharmaceutical company with an equity grant and is required to make tiered royalty payments based on net sales of all products licensed under the agreement in the low single-digit percentages. In conjunction with the Collaboration, the Company initially issued 886,305 Series A Preferred Units (“Series A Preferred Units”) to the pharmaceutical company. On November 1, 2018, these Series A Preferred Units were exchanged on a one-for-one basis for shares of Series A Convertible Preferred Stock (the “Series A Preferred Stock”). These shares vest in equal installments over three years. The Company is recording expense over the remaining vesting period based on the fair value of the shares under the Collaboration. The Company recorded \$0.3 million and \$0.4 million to research and development expense related to the vesting of 166,183 and 221,579 shares of Series A Preferred Stock during the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, all shares under the Collaboration were fully vested and all expense had been recognized.

The royalty payments are contingent and as such are not being recorded until incurred. The Company determined that the license is representative of an in-process research and development asset, with no future alternative use. As such, the Company records the expense related to the vesting of shares as research and development expense in the Company’s consolidated statements of operations and comprehensive loss.

The Collaboration can be terminated by either party for convenience with 60-days written notice and may also be terminated in the event of a material breach.

The following table presents the changes in accounts receivable, contract assets and liabilities for the year ended December 31, 2020 (in thousands)

	<u>Balance at December 31, 2019</u>	<u>Additions</u>	<u>Deductions</u>	<u>Balance at December 31, 2020</u>
Accounts receivable and contract assets:				
Billed receivables – Sanofi	\$ —	\$ 150,577	\$ (150,000)	\$ 577
Unbilled receivables – Sanofi	—	1,433	(577)	856
Total accounts receivable and contract assets	<u>\$ —</u>	<u>\$ 152,010</u>	<u>\$ (150,577)</u>	<u>\$ 1,433</u>
Contract Liabilities:				
Deferred Revenue – Vertex	\$ 52,991	\$ —	\$ (15,243)	\$ 37,748
Deferred Revenue – Sanofi	—	151,433	(18,791)	132,642
Total contract liabilities	<u>\$ 52,991</u>	<u>\$ 151,433</u>	<u>\$ (34,034)</u>	<u>\$ 170,390</u>

Note 6. Property and equipment

Property and equipment consist of the following as of December 31, 2020 and 2019 (in thousands):

	December 31, 2020	December 31, 2019
Lab and office equipment under and financing right-of-use asset	\$ 2,771	\$ 2,751
Lab equipment	1,636	919
Computer equipment	89	71
Furniture & fixtures	861	104
Leasehold improvements	7,599	545
Assets not yet in service	32	453
Total property and equipment	12,988	4,843
Less accumulated depreciation	(2,147)	(1,049)
Property and equipment, net	<u>\$ 10,841</u>	<u>\$ 3,794</u>

Depreciation expense for the years ended December 31, 2020 and 2019 was \$1.8 million and \$0.9 million, respectively.

Included in property and equipment is lab and office equipment right-of-use assets under financing leases with a cost basis of \$2.8 million and accumulated amortization expense of \$1.2 million and \$0.5 million as of December 31, 2020 and 2019.

Amortization expense related to right-of-use assets was \$0.7 million and \$0.4 million the years ended December 31, 2020 and 2019 and is included in depreciation expense.

Note 7. Leases

In February 2018, the Company entered into a noncancelable facility lease agreement (the "Lease") for 9,836 square feet of research and development and office space in Cambridge, Massachusetts. In March 2020, the Company signed a termination agreement for this lease which was determined to be a lease modification that resulted in a reduction of the right-of-use asset and liability of \$2.2 million. The lease termination was effective July 31, 2020 and the Company no longer has any obligations under the Lease.

In accordance with the lease agreement, the Company was required to maintain a security deposit and provided a letter of credit to the landlord for \$0.2 million, which was recorded in other assets as of December 31, 2019. In October 2020, the Company was released from the security deposit and letter of credit and collected the \$0.2 million previously classified in other current assets.

In April 2019, the Company entered into a facility sublease agreement (the "Sublease") for 1,471 square feet of office space in Cambridge, Massachusetts. The term of the lease began on June 24, 2019 and terminated on June 30, 2020, and following termination, the Company had no further obligations under the Sublease. The Sublease required the Company to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts were considered variable lease costs and, therefore, are not included in the measurement of the lease and are instead recognized to expense as incurred.

In October 2019, the Company entered into a noncancelable facility lease agreement (the "New Lease") for 34,522 square feet of research and development and office space in Watertown, Massachusetts. The term of the New Lease is 120 months and expires on March 31, 2030. The New Lease has an option to be extended for an additional five years. The lease is not reasonably certain to be extended and as such the additional term is not included in the measurement of the lease. The New Lease includes a rent escalation clause, and rent expense is being recorded on a straight-line basis. The Company received a tenant incentive allowance of \$5.5 million in 2020 as the tenant improvements were completed all of which has been collected from its landlord as of December 31, 2020. In accordance with the lease agreement, the Company is required to maintain a security deposit and provided a letter of credit to the landlord for \$1.6 million, which is recorded in other assets as of December 31, 2020.

The Company's financing lease obligations consist of certain property and equipment financed through capital leases.

The components of the lease costs for the years ended December 31, 2020 and 2019 (in thousands):

	Year ended December 31,	
	2020	2019
Operating lease costs	\$ 2,719	\$ 1,597
Financing lease costs:		
Amortization of right-to-use assets, financing leases	716	385
Interest expense for financing lease liabilities	121	46
Variable lease costs	621	340
Total lease costs	<u>\$ 4,177</u>	<u>\$ 2,368</u>

Supplemental cash flow information relating to the Company's leases for the years ended December 31, 2020 and 2019 was as follows (in thousands):

	Year ended December 31,	
	2020	2019
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows used in (provided by) operating leases	\$ (3,024)	\$ 635
Operating cash flows used in finance leases	\$ 587	\$ 46
Financing cash flows used in finance leases	\$ 121	\$ 385

Weighted average remaining lease terms and discount rates as of December 31, 2020 and 2019 were as follows:

	Year ended December 31,	
	2020	2019
Remaining lease term:		
Operating lease	9.3	9.3
Financing lease	2.8 Years	3.7 Years
Discount Rate:		
Operating lease	10.5%	10.3%
Financing lease	8.0%	7.8%

The undiscounted future lease payments for operating and finance leases as of December 31, 2020, were as follows (in thousands):

Fiscal Year	Operating Leases	Financing Leases
2021	2,691	712
2022	2,581	459
2023	2,659	245
2024	2,732	—
2025	2,814	—
Thereafter	12,925	—
Total minimum lease payments	<u>26,402</u>	<u>1,416</u>
Less amounts representing interest or imputed interest	<u>(9,702)</u>	<u>(123)</u>
Present value of lease liabilities	<u>\$ 16,700</u>	<u>\$ 1,293</u>

Note 8. Accrued Expenses

Accrued expenses consist of the following as of December 31, 2020 and 2019 (in thousands):

	Year ended December 31,	
	2020	2019
Research and development expenses	\$ 5,821	\$ 2,617
Payroll and payroll-related	2,918	1,256
Professional fees	1,585	606
Other	6	89
Accrued expenses	\$ 10,330	\$ 4,568

Note 9. Other Commitments and Contingencies

In the ordinary course of business, the Company may be subject to legal proceedings, claims and litigation as the Company operates in an industry susceptible to patent legal claims. The Company accounts for estimated losses with respect to legal proceedings and claims when such losses are probable and estimable. Legal costs associated with these matters are expensed when incurred. The Company is not currently a party to any legal proceedings.

Indemnification Arrangements

As permitted under Delaware law, the Company has agreements whereby it indemnifies its investors, employees, officers, and directors (collectively, the "Indemnified Parties") for certain events or occurrences while the Indemnified Parties are, or were serving, at its request in such capacity. The term of the indemnification period is for the Indemnified Parties' lifetime. The Company believes the estimated fair value of these indemnification agreements is minimal. The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to these agreements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners or customers, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to the Company's products. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations as of December 31, 2020 or 2019.

Note 10. Convertible Preferred Stock

Immediately prior to the IPO, the Company's Articles of Association (the "Articles"), as further amended and restated (the "2018 Amended Articles"), authorized a total of 52,483,788 convertible preferred stocks with a par value of \$0.0001 per share, of which 3,000,000 shares have been designated as Series Seed Preferred Stock, 14,886,305 shares have been designated as Series A Preferred Stock, 16,009,845 shares have been designated as Series B Preferred Stock, 3,059,695 shares have been designated as Series B-1 Preferred Stock and 15,527,943 shares have been designated as Series C Preferred Stock. The Series A, Series B, Series B-1 and Series C convertible preferred stocks will be collectively referred to as the Convertible Preferred Stock.

In January 2020, the Company issued 1,182,265 shares of Series B Preferred Stock at \$4.06 per share to complete the second closing of the Series B Preferred Stock issuance for total proceeds of \$4.8 million. The issuance costs related to the second tranche were insignificant.

In March 2020, the Company executed a Series C Preferred Stock Purchase Agreement (the "Series C SPA") to issue 13,539,141 shares of Series C Preferred Stock at a purchase price of \$6.5366 per share for a total consideration of \$88.2 million, net of issuance costs of \$0.3 million. In conjunction with the Series C SPA, the Company exchanged 1,988,802 shares of Series A Preferred Stock for an equal number of shares of Series C Preferred Stock related to a transaction amongst investors. This resulted in a total issuance of 15,527,943 shares of Series C Preferred Stock. The fair value of the shares of Series C Preferred Stock issued exceeded the carrying value of the shares of Series A Preferred Stock exchanged by \$9.1 million, which was recognized as a deemed dividend through a reduction of \$2.3 million to additional paid-in capital and an increase of \$6.7 million to the accumulated deficit. The \$9.1 million deemed dividend increased the net loss for the year ending December 31, 2020 to arrive at net loss attributable to common stockholders in the calculation of earnings per share.

In connection with the Company's August 21, 2020, IPO all issued and outstanding Convertible Preferred Stock of 50,439,595 were converted to 31,625,534 shares of the Company's common stock and are no longer issued or outstanding as of December 31, 2020.

Note 11. Equity-Based Compensation

2018 Stock Option and Grant Plan

In November 2018, the Company adopted, and its stockholders approved, the 2018 Stock Option and Grant Plan (the “2018 Plan”), which provides for the granting of stock options and other equity-based awards at the discretion of the Board of Directors or any subcommittee of the Board of Directors to its employees, officers, directors, and independent contractors. No further grants will be made under the 2018 Plan. However, the 2018 Plan will continue to govern outstanding equity awards granted thereunder. To the extent outstanding options granted under the 2018 Plan are cancelled, forfeited or otherwise terminated without being exercised and would otherwise have been returned to the share reserve under the 2018 Plan, the number of shares underlying such awards will be available for future grant under the 2020 Stock Option and Incentive Plan. Following the completion of the Company’s initial public offering no additional shares will be granted under the 2018 Plan. However, the 2018 Plan will continue to govern outstanding equity awards granted thereunder.

2020 Stock Option and Incentive Plan

In August 2020, the Company and its stockholders approved the 2020 Stock Option and Incentive Plan (the “2020 Plan”), which became effective on August 20, 2020. The 2020 Plan replaced the 2018 Plan as the Company’s board of directors has determined not to make additional awards under the 2018 Plan following the closing of the Company’s IPO. The 2020 Plan allows the Company to make equity-based and cash-based incentive awards to its officers, employees, directors and consultants. The Company has initially reserved 4,457,370 shares of its common stock for the issuance of awards under the 2020 Plan, which includes the shares of common stock remaining available for issuance under its 2018 Plan as of the business day immediately prior to the effective date of the registration statement. The 2020 Plan provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2021 and each January 1 thereafter, by 4% of the Company’s outstanding number of shares of common stock on the immediately preceding December 31, or such lesser number of shares as determined by the Company’s compensation committee. These limits are subject to adjustment in the event of a stock split, stock dividend or other change in the Company’s capitalization. As of December 31, 2020, there were an aggregate of 3,148,671 shares remaining available for future grants.

2020 Employee Stock Purchase Plan

In August 2020, the Company and its stockholders approved the 2020 Employee Stock Purchase Plan (the “2020 ESPP”), which became effective August 20, 2020. The 2020 ESPP initially reserves and authorizes the issuance of up to a total of 445,653 shares of common stock to participating employees. The 2020 ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2021 and each January 1 thereafter through January 1, 2030, by the least of (i) 438,898 shares of common stock, (ii) 1% of the Company’s outstanding number of shares of common stock on the immediately preceding December 31 or (iii) such lesser number of shares of common stock as determined by the administrator of the 2020 ESPP. The number of shares reserved under the 2020 ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in the Company’s capitalization. As of December 31, 2020, there were an aggregate of 445,653 shares remaining available for future grants.

Stock Options

A summary of stock option activity under the 2020 Stock Option and Grant Plan during the year ended December 31, 2020 is as follows (in thousands except share and per share data):

	Number of Options Outstanding	Weighted Average Strike Price per Option	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2019	2,945,297	\$ 2.03	8.93	\$ 7,798
Granted	3,213,204	13.22		
Exercised	(78,852)	2.06		
Forfeited	(246,937)	2.55		
Outstanding at December 31, 2020	5,832,712	\$ 8.17	9.08	\$ 314,001
Exercisable at December 31, 2020	1,580,924	\$ 3.38	8.76	\$ 92,674

The intrinsic value of stock options exercised during the years ended December 31, 2020 and 2019 was \$1.6 million, \$0.1 million, respectively.

The weighted-average fair value of options granted during the years ended December 31, 2020 and 2019 was \$8.35 and \$1.69 per share, respectively.

As of December 31, 2020, the total unrecognized stock-based compensation expense for unvested stock options was \$25.6 million, which is expected to be recognized over 3.3 years. The total fair value of stock options vested during the years ended December 31, 2020 and 2019 was \$4.0 million, \$0.2 million, respectively.

The following table outlines our equity-based compensation expense for stock options for the years ended December 31, 2020 and 2019:

	<u>Year ending December 31,</u>	
	<u>2020</u>	<u>2019</u>
Research and development	\$ 2,084	\$ 380
General and administrative	2,864	212
Total equity-based compensation	<u>\$ 4,948</u>	<u>\$ 592</u>

The weighted-average assumptions that the Company used in Black-Scholes option pricing model to determine the grant date fair value of stock options granted to employees and non-employees for the years ended December 31, 2020 and 2019:

	<u>Year ending December 31,</u>	
	<u>2020</u>	<u>2019</u>
Expected term (in years)	6.09	6.49
Volatility	70%	71%
Risk-free interest rate	0.5%	1.83%
Dividend yield	0.00%	0.00%

Restricted Common Stock

The Company has granted shares of restricted common stock with service-based and performance-based vesting conditions. A summary of restricted stock activity under the 2018 Plan during the year ended December 31, 2020 is as follows:

	<u>Number of Units Outstanding</u>	<u>Grant Date Fair Value per Share</u>
Unvested at December 31, 2019	232,434	\$ 1.60
Granted	—	—
Vested	(102,651)	1.60
Forfeited	(19,679)	1.60
Unvested at December 31, 2020	<u>110,104</u>	<u>\$ 1.60</u>

There were no grants of restricted stock during the years ended December 31, 2020 and 2019.

As of December 31, 2020, the total unrecognized stock-based compensation expense for unvested restricted stock was \$0.3 million, which is expected to be recognized over 1.6 years. The total fair value of restricted stock vested during the years ended December 31, 2020 and 2019 was \$0.1 million and \$0.5 million, respectively.

During the years ended December 31, 2020 and 2019, the Company recorded stock-based compensation expense for restricted stock of \$0.2 million and \$0.4 million, of which \$0.2 million and \$0.2 million was included in research and development expense and an immaterial amount and \$0.2 million was included in general and administrative expense, respectively. Included within the 2019 general and administrative stock-based compensation expense was \$0.1 million from a modification of an employee's awards.

Equity-Based Compensation Expense

Total equity-based compensation expense recorded as research and development and general and administrative expenses for employees, directors, and non-employees during the years ended December 31, 2020 and 2019 is as follows (in thousands):

	Years ending December 31,	
	2020	2019
Research and development	\$ 2,305	\$ 688
General and administrative	2,885	508
Total equity-based compensation	\$ 5,190	\$ 1,196

Note 12. Related-Party Transactions

In addition to the collaboration discussed in Note 5, the Company had the following related party transactions for the periods presented in the accompanying consolidated financial statements, which has not otherwise been discussed in these notes to the consolidated financial statement. The Company made payments of \$0.8 million and \$1.0 million to an investor for rent expenses for the years ended December 31, 2020 and 2019, respectively.

Note 13. Income Taxes

The Company records income tax expense related to profits realized by its U.S. operating subsidiaries. For the years ended December 31, 2020 and 2019, no income tax expense was recorded due the group's net operating loss ("NOL") and full valuation allowance.

The rate reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate for the years ended December 31, 2020 and 2019 are as follows:

	December 31,	
	2020	2019
Tax effect at statutory rate	21.0%	21.0%
State taxes	5.8%	7.0%
Stock compensation	(0.9%)	(0.6%)
Permanent differences	0.0%	0.0%
Federal research and development credits	3.6%	2.0%
Other	(0.7%)	0.0%
Change in valuation allowance	(28.8%)	(29.4%)
Total	0.0%	0.0%

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's net deferred income taxes are as follows (in thousands):

	December 31,	
	2020	2019
<i>Deferred Tax Assets:</i>		
Federal net operating loss carryforwards	\$ 15,621	\$ 15,011
State net operating loss carryforwards	3,866	4,319
Research and development credit carryforwards	3,757	1,637
Lease liabilities	4,563	5,286
Deferred revenue	10,313	—
Accruals and reserves, stock and other	1,589	525
Total deferred tax assets	\$ 39,709	\$ 26,778
Valuation allowance	\$ (34,075)	\$ (20,949)
Deferred tax assets	\$ 5,634	\$ 5,829
Fixed and intangible assets	(1,506)	(754)
Right-of-use assets	(4,128)	(5,075)
Net deferred tax asset	\$ —	\$ —

As required by ASC 740, management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are composed principally of NOL carryforwards and research and development credit carryforwards. Management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, and, as a result, a valuation allowance of \$34.1 million and \$20.9 million has been established at December 31, 2020 and 2019, respectively. During 2020, the valuation allowance increased by \$13.1 million primarily due to the increase in the Company's NOL during the period.

The Company has incurred NOLs from inception. At December 31, 2020 and 2019, the Company has federal NOL carryforwards of approximately \$74.4 million and \$71.5 million, respectively, and state NOL carryforwards of approximately \$61.2 million and \$68.3 million, respectively. Of the federal net operating loss carryovers, \$64.6 million is not subject to expiration and the remaining federal and state NOLs begin to expire in 2036. These loss carryforwards are subject to review and possible adjustment by the appropriate taxing authorities.

Utilization of net operating loss and research and development credit carryforwards may generally be subject to limitation under Sections 382 and 383 of the Internal Revenue Code due to ownership changes that have occurred previously, or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset any post-ownership change taxable income and tax, respectively. The latest Section 382 study was performed through December 31, 2020, noting that a historic ownership change has likely occurred. Nonetheless, the Company has determined that as of December 31, 2020 the prospective utilization of all net operating loss and tax credit carryforwards generated from inception through December 31, 2020, and therefore the corresponding Federal and Massachusetts deferred tax assets, should not be restricted by Sections 382 and 383, although ownership changes after December 31, 2020 could impact the Company's ability to utilize these tax attributes in the future.

At December 31, 2020 and 2019, the Company had federal research and development credit carryforwards of \$2.7 million and \$1.1 million, respectively, and state research and development credit carryforwards of \$1.3 million and \$0.7 million, respectively. These carryforwards begin to expire in 2036.

The Company follows the provisions of ASC 740-10, "Accounting for Uncertainty in Income Taxes," which specifies how tax benefits for uncertain tax positions are to be recognized, measured, and recorded in financial statements; requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the balance sheet; and provides transition and interim period guidance, among other provisions. As of December 31, 2020, and 2019, the Company has not recorded any amounts for uncertain tax positions. The Company's policy is to recognize interest and penalties accrued on any uncertain tax positions as a component of income tax expense, if any, in its statements of income. As of December 31, 2020 and 2019, the Company had no reserves for uncertain tax positions. For the years ended December 31, 2020 and 2019, no estimated interest or penalties were recognized on uncertain tax positions.

The Company's tax returns for the years ended December 31, 2017 to December 31, 2020 remain open and subject to examination by the Internal Revenue Service and state taxing authorities.

Note 14. Net Loss per Share

Net Loss per Share

Basic and diluted loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average common shares outstanding (in thousands, except for share and per share data):

	<u>December 31,</u>	
	<u>2020</u>	<u>2019</u>
Numerator:		
Net loss	\$ (45,593)	\$ (41,246)
Deemed dividend from exchange of convertible preferred stock	(9,050)	—
Net loss attributable to common stockholders	<u>\$ (54,643)</u>	<u>\$ (41,246)</u>
Denominator:		
Weighted average common shares outstanding, basic and diluted	17,349,582	1,698,522
Net loss per share, basic and diluted	<u>\$ (3.15)</u>	<u>\$ (24.28)</u>

The Company's potentially dilutive securities, which include convertible preferred stock, restricted stock, and stock options, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following from the computation of diluted net loss per share attributable to common stockholders at December 31, 2020 and 2019 because including them would have had an anti-dilutive effect:

	December 31,	
	2020	2019
Convertible Preferred Stock	—	22,325,780
Unvested Restricted Stock	110,104	232,434
Options to purchase Common Stock	1,580,924	2,945,298
Total	<u>1,691,028</u>	<u>25,503,512</u>

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.**Management's Evaluation of Disclosure Controls and Procedures**

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer, who serves as our principal executive officer, and our Chief Financial Officer, who serves as our principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020, the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our chief executive officer and chief financial officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Internal Control Over Financial Reporting***Management's Report on Internal Control Over Financial Reporting***

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control Over Financial Reporting

None.

Item 9B. Other Information.

The registrant must disclose under this item any information required to be disclosed in a report on Form 8-K during the fourth quarter of the year covered by this Form 10-K, but not reported, whether or not otherwise required by this Form 10-K. If disclosure of such information is made under this item, it need not be repeated in a report on Form 8-K which would otherwise be required to be filed with respect to such information or in a subsequent report on Form 10-K.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) *Financial Statements*

For a list of the consolidated financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, which is incorporated into this Item by reference.

(b) *Exhibits*

Exhibit Number	Description
3.1	<u>Fourth Amended and Restated Certificate of Incorporation of Kymera Therapeutics, Inc. (Incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on August 25, 2020).</u>
3.2	<u>Second Amended and Restated Bylaws of Kymera Therapeutics, Inc. (Incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on August 25, 2020).</u>
4.1	<u>Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-240264) filed with the Securities and Exchange Commission on August 17, 2020).</u>
4.2	<u>Second Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, effective as of March 11, 2020 (Incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-240264) filed with the Securities and Exchange Commission on July 31, 2020).</u>
4.3	<u>Description of Securities</u>
10.1#	<u>2018 Stock Option and Grant Plan, and form of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-240264) filed with the Securities and Exchange Commission on July 31, 2020).</u>
10.2#	<u>2020 Stock Option and Incentive Plan, and form of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1/A (File No. 333-240264) filed with the Securities and Exchange Commission on August 17, 2020).</u>
10.3#	<u>Non-Employee Director Compensation Policy (Incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1/A (File No. 333-240264) filed with the Securities and Exchange Commission on August 13, 2020).</u>
10.4#	<u>Senior Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333-240264) filed with the Securities and Exchange Commission on August 13, 2020).</u>
10.5#	<u>Amended and Restated 2020 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 5, 2020).</u>
10.6	<u>Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (Incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1/A (File No. 333-240264) filed with the Securities and Exchange Commission on August 17, 2020).</u>
10.7	<u>Lease Agreement between the Registrant and ARE-TECH SQUARE, LLC, dated as of February 28, 2018 (Incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1 (File No. 333-240264) filed with the Securities and Exchange Commission on July 31, 2020).</u>
10.8	<u>Lease between the Registrant and Arsenal Yards Holding LLC, dated as of August 15, 2019 (Incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-240264) filed with the Securities and Exchange Commission on July 31, 2020).</u>

10.9#	<u>Form of Amended and Restated Employment Agreement (Incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1/A (File No. 333-240264) filed with the Securities and Exchange Commission on August 13, 2020).</u>
10.10†	<u>Master Collaboration Agreement between the Registrant and Vertex Pharmaceuticals Incorporated, dated as of May 9, 2019 (Incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1 (File No. 333-240264) filed with the Securities and Exchange Commission on July 31, 2020).</u>
10.11†	<u>Collaboration Agreement between the Registrant and GlaxoSmithKline Intellectual Property Development Limited, dated as of October 3, 2017 (Incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1/A (File No. 333-240264) filed with the Securities and Exchange Commission on August 5, 2020).</u>
10.12†	<u>Collaboration and License Agreement between the Registrant and Genzyme Corporation, dated as of July 7, 2020 (Incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-240264) filed with the Securities and Exchange Commission on July 31, 2020).</u>
10.13†	<u>First Amendment to Collaboration Agreement between the Registrant and GlaxoSmithKline Intellectual Property Development Limited, dated as of August 27, 2020 (Incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 5, 2020).</u>
10.14	<u>First Amendment to Master Collaboration Agreement between the Registrant and Vertex Pharmaceuticals Incorporated, dated as of August 27, 2020 (Incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 5, 2020).</u>
21.1	<u>List of Subsidiaries of Registrant.</u>
23.1	<u>Consent of Ernst & Young LLP, independent registered public accounting firm.</u>
24.1	<u>Power of Attorney (included on signature page to this Annual Report on Form 10-K).</u>
31.1	<u>Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
31.2	<u>Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
32.1±	<u>Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
32.2±	<u>Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

+ This certification will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, except to the extent specifically incorporated by reference into such filing.

Indicates a management contract or any compensatory plan, contract or arrangement.

† Application has been made to the Securities and Exchange Commission for confidential treatment of certain provisions. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.

(c) Financial Statement Schedules

No financial statements have been submitted because they are not required or are not applicable or because the information required is included in the consolidated financial statements or the notes thereto.

Item 16. Form 10-K Summary

None.

**Description of the Registrant's Securities Registered Pursuant to
Section 12 of the Securities Exchange Act of 1934, as amended**

The common stock, par value \$0.0001 per share ("Common Stock"), of Kymera Therapeutics, Inc. ("Kymera," "we," or "our") is registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The following description sets forth certain general terms and provisions of our Common Stock. These descriptions are in all respects subject to and qualified in their entirety by, and should be read in conjunction with, the applicable provisions of our Amended and Restated Certificate of Incorporation (our "Charter") and our Amended and Restated By-laws (our "By-laws"), each of which is incorporated herein by reference and copies of which are incorporated by reference as exhibits to our most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, and the applicable provisions of General Corporation Law of the State of Delaware (the "DGCL").

Authorized Capital Stock

We are authorized to issue 150,000,000 shares of Common Stock and 10,000,000 shares of preferred stock, par value \$0.0001 per share ("Preferred Stock").

Common Stock

The holders of Common Stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of Common Stock do not have any cumulative voting rights. Holders of Common Stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. The Common Stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of Common Stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding Preferred Stock.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of Preferred Stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of Common Stock. The issuance of our Preferred Stock could adversely affect the voting power of holders of Common Stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of Preferred Stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action.

Registration Rights

Pursuant to the terms of our Second Amended and Restated Investors' Rights Agreement, dated as of March 11, 2020, with certain of our stockholders (the "Investors' Rights Agreement"), certain of our stockholders are entitled to rights with respect to the registration of their shares (which we refer to herein as "registrable securities") under the Securities Act of 1933, as amended (the "Securities Act"), including demand registration rights, short-form registration rights and piggyback registration rights.

Demand Registration Rights

The holders of our registrable securities are entitled to demand registration rights. Under the terms of the Investors' Rights Agreement, upon the written request of holders of at least 55% of these securities, which must include (i) at least one Major Series A Investor, (ii) at least one Major Series B Investor and (iii) at least one Major Series C Investor, as such terms are defined in the Investors' Rights Agreement, to file a registration statement and use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the investors' rights agreement.

Short-Form Registration Rights

The holders of our registrable securities are entitled to short-form registration rights. Pursuant to the Investors' Rights Agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of holders of at least 5% of the Registrable Securities then outstanding, as such term is defined in the Investors' Rights Agreement at an aggregate offer price of at least \$2.0 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve month period. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the Investors' Rights Agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of our outstanding registrable securities are entitled to include their shares in the registration. Subject to certain exceptions contained in the Investors' Rights Agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

The Investors' Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The registration rights granted under the Investors' Rights Agreement will terminate the earliest to occur of: (i) on the fifth anniversary of the our initial public offering, (ii) at such time after our initial public offering when all registrable securities could be sold under Rule 144 of the Securities Act or another similar exemption without restriction within a three-month period or (iii) a merger, sale or liquidation of our company.

Anti-Takeover Effects of Delaware Law and Certain Provisions of our Charter and By-Laws

Our Charter and By-Laws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our Charter provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our Charter also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our Charter provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our By-Laws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our Charter and By-Laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our By-Laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our By-Laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our By-Laws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Charter and By-Laws

Any amendment of our Charter must first be approved by a majority of our board of directors, and if required by law or our Charter, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our By-Laws and Charter must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than a majority of the outstanding shares of each class entitled to vote thereon as a class. Our By-Laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the By-Laws; and may also be amended by the affirmative vote of at least two-thirds of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the

amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our Charter provides for 10,000,000 authorized shares of Preferred Stock. The existence of authorized but unissued shares of Preferred Stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of Preferred Stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our Charter grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of Preferred Stock. The issuance of shares of Preferred Stock could decrease the amount of earnings and assets available for distribution to holders of shares of Common Stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the DGCL. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; or

- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Choice of Forum

Our By-Laws provide that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware (or, if the Chancery Court does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (iii) any action asserting a claim against us, or any current or former director, officer, or other employee or stockholder, arising out of or pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or By-Laws; and (iv) any action asserting a claim against us or any current or former director or officer or other employee governed by the internal affairs doctrine; provided, however, that this choice of forum provision does not apply to any causes of action arising under the Securities Act or the Exchange Act. Our By-Laws further provide that, unless we consent in writing to an alternative forum, the United States District Court for the District of Massachusetts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Our By-Laws also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision.

We recognize that the forum selection clause in our By-Laws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts, as applicable. Additionally, the forum selection clause in our By-Laws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Court of Chancery of the State of Delaware or the United States of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Stock Exchange Listing

Our Common Stock is listed on The Nasdaq Global Market under the trading symbol "KYMR."

Transfer Agent and Registrar

The Transfer Agent and Registrar for our Common Stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-428.

SUBSIDIARIES

Subsidiary
Kymera Securities Corporation

Jurisdiction of Incorporation
Massachusetts

ACTIVE/107610297.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statement (Form S-8 No. 333- 248249) pertaining to the Kymera Therapeutics, Inc. 2018 Stock Option and Grant Plan, Kymera Therapeutics, Inc. 2020 Stock Option and Incentive Plan, and Kymera Therapeutics, Inc. 2020 Employee Stock Purchase Plan of our report dated March 11, 2021, with respect to the consolidated financial statements of Kymera Therapeutics, Inc. included in this Annual Report (Form 10-K) of Kymera Therapeutics, Inc. for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 11, 2021

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Kymera Therapeutics, Inc. (the "Company") on Form 10-K for the period ending December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 11, 2021

By: _____ /s/ Nello Mainolfi, Ph.D.
Nello Mainolfi, Ph.D.
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Kymera Therapeutics, Inc. (the "Company") on Form 10-K for the period ending December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 11, 2021

By: _____ /s/ Bruce Jacobs, CFA, MBA
Bruce Jacobs, CFA, MBA
Chief Financial Officer
(Principal Financial Officer)