TRICIDA

2020 Annual Report

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: 001-38558

TRICIDA

TRICIDA, INC.
(Exact name of registrant as specified in its charter)

Delaware	**46-3372526**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

7000 Shoreline Court, Suite 201
South San Francisco, California 94080
(415) 429-7800
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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 $0.001 per share	TCDA	The Nasdaq Global Select 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 Section 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, a 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	☒	Accelerated filer	☐	Non-accelerated filer	☐
Smaller reporting company	☐	Emerging growth company	☐		

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 ☒

As of June 30, 2020 (the last business day of the registrant's most recently completed second fiscal quarter), the aggregate market value of the common stock held by non-affiliates of the registrant was approximately $0.8 billion, based on the closing price of the common stock as reported on the Nasdaq Global Select Market on that date. Shares of common stock held by each person who is known to own 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates of the Company. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

On February 19, 2021, the registrant had 50,244,465 shares of common stock, par value $0.001 per share, outstanding.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. Forward-looking statements generally can be identified by words such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “potential,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- estimates of our expenses, capital requirements and our needs for additional financing;
- the prospects of veverimer (also known as TRC101), our only investigational drug candidate, which is still in development;
- our ability to obtain approval of our New Drug Application, or NDA, for veverimer from the U.S. Food and Drug Administration, or FDA, under either traditional approval or the Accelerated Approval Program, if at all;
- our ability to resolve the deficiencies identified by the FDA in the Complete Response Letter and issues raised in the Appeal Denied Letter related to our NDA for veverimer;
- our expectations regarding the timing of the completion of any nonclinical or clinical study;
- the design of our renal outcomes trial, VALOR-CKD (also known as TRCA-303), including the sample size, trial duration, endpoint definition, event rate assumptions and eligibility criteria;
- our expectations regarding the timing and location of the enrollment, distribution of enrollment across geographical regions, endpoint accrual, completion, outcome and reporting of results of our ongoing VALOR-CKD trial;
- the outcome and results of our ongoing VALOR-CKD trial;
- the market acceptance or commercial success of veverimer, if approved, and the degree of acceptance among physicians, patients, patient advocacy groups, health care payers and the medical community;
- our expectations regarding competition, potential market size and the size of the patient population for veverimer, if approved for commercial use;
- our expectations regarding our ability to satisfy our covenants under our credit facility with Hercules Capital, Inc. and Hercules Technology III, L.P.;
- our expectations regarding the safety, efficacy and clinical benefit of veverimer;
- our ability to achieve and maintain regulatory approval of veverimer, and any related requirements, restrictions, limitations and/or warnings in the label of veverimer;
- our sales, marketing or distribution capabilities and our ability to commercialize veverimer, if we obtain regulatory approval;
- our current and future agreements with third parties in connection with the manufacturing, commercialization, packaging and distribution of veverimer;
- our expectations regarding the ability of our contract manufacturing partners to produce veverimer in the quantities and timeframe that we will require;
- our expectations regarding our future costs of goods;
- our ability to attract, retain and motivate key personnel;

- the scope of protection we are able to establish and maintain for intellectual property rights covering veverimer;
- potential claims relating to our intellectual property and third-party intellectual property;
- the duration of our intellectual property estate that will provide protection for veverimer;
- our ability to establish collaborations in lieu of obtaining additional financing;
- the potential impact of pandemics, including COVID-19, on the health care system, financial markets and economy generally and on our business in particular; and
- our financial performance.

These forward-looking statements are based on management’s current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management’s beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Item 1A. “Risk Factors” and elsewhere in this Annual Report on Form 10-K. Investors in our securities are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K. 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. Investors in our securities should, however, review the factors and risks we describe in the reports we will file from time to time with the Securities and Exchange Commission after the date of this Annual Report on Form 10-K.

PART I

ITEM 1. BUSINESS

Overview

Our goal is to slow the progression of chronic kidney disease, or CKD, through the treatment of metabolic acidosis. We are a pharmaceutical company focused on the development and commercialization of our investigational drug candidate, veverimer (also known as TRC101), a non-absorbed, orally-administered polymer designed to treat metabolic acidosis by binding and removing acid from the gastrointestinal, or GI, tract. Metabolic acidosis is a serious condition commonly caused by CKD and is believed to accelerate the progression of kidney deterioration. It can also lead to bone loss, muscle wasting and impaired physical function. Metabolic acidosis in patients with CKD is typically a chronic disease and, as such, requires long-term treatment to mitigate its deleterious consequences.

There are currently no FDA-approved therapies for treating chronic metabolic acidosis. We estimate that metabolic acidosis affects approximately 3 million patients with CKD in the United States, and we believe that treating metabolic acidosis and slowing the progression of CKD in patients with metabolic acidosis and CKD represents a significant unmet medical need and market opportunity.

Veverimer is an in-house discovered, new chemical entity. We have a broad intellectual property estate that we believe will provide patent protection for veverimer until at least 2038 in the United States, at least 2035 in Europe and Russia, and at least 2034 in Australia, China, Hong Kong, Israel, Japan, Mexico and certain other markets.

Metabolic acidosis observed in patients with CKD is most often caused by an imbalance in acid production relative to acid excretion. The human body generates acid every day through normal food intake and metabolism. Sources of acid include amino acids and nucleic acids from daily dietary intake and digestion of proteins. The daily load of nonvolatile acids from metabolic processes amounts to approximately 1 milliequivalent, or mEq, per kilogram, or kg, of body weight, or 50 to 100 mEq per day for adults. A healthy kidney excretes this acid daily, but in patients with CKD acid excretion is compromised, and as a result, acid accumulates in the body. Over time, a vicious cycle of worsening metabolic acidosis and accelerated progression of kidney disease can result.

Patients with CKD are often frail and have impaired physical function, and metabolic acidosis is one factor that has been implicated as a potential contributor. Metabolic acidosis has direct effects on skeletal muscle catabolism and bone demineralization. Two large retrospective cohort analyses found that low serum bicarbonate level was independently associated with adverse health outcomes related to physical functioning, such as gait speed, quadriceps strength, failure to thrive and fractures/falls (Abramowitz et al., 2011; Reaven et al., 2019). Several prospective studies of patients with metabolic acidosis and CKD have shown that treatment of metabolic acidosis can increase muscle mass (de Brito-Ashurst et al., 2009; Dubey et al., 2018) and improve muscle function (Abramowitz et al., 2013) and physical function related quality of life (de Brito-Ashurst et al., 2015).

Acid binding in the GI tract is a novel approach to treating metabolic acidosis without introducing deleterious counterions or metals. This approach mimics the physiologic response to acid removal seen with persistent vomiting or nasogastric suction that results in an elevated serum bicarbonate level. To achieve the desired effect of increasing serum bicarbonate with a convenient daily dose of less than 10 grams per day, an acid binding polymer should have an amine capacity to bind at least 5 mEq of proton/gram. Once protonated, the acid binding polymer needs to preserve the effect of the proton binding by not removing anions such as fatty and bile acids that represent precursors metabolized to bicarbonate in the blood. The complementary anion to be bound that ensures net acid removal from the GI tract is chloride, the smallest anion present in the GI tract.

Veverimer is a low-swelling, spherical polymer bead that is approximately 100 micrometers in diameter. It is a single, high molecular weight, crosslinked polyamine molecule. The size of veverimer prevents systemic absorption from the GI tract. The high degree of cross-linking within veverimer limits swelling and the overall volume in the GI tract, with the goal of facilitating good GI tolerability. The high amine content of veverimer provides proton binding capacity of approximately 10 mEq/gram of polymer. The size exclusion built into the three-dimensional structure of the polymer enables preferential binding of chloride versus larger inorganic and organic anions, including phosphate, citrate, fatty acids and bile acids. This size exclusion mechanism allows a majority of the binding capacity to be used for hydrochloric acid binding.

We are currently conducting a renal outcomes clinical trial, VALOR-CKD (also known as TRCA-303), to determine if veverimer slows CKD progression in patients with metabolic acidosis associated with CKD. Our VALOR-CKD trial is a randomized, double-blind, placebo-controlled, time-to-event trial. The primary endpoint event in VALOR-CKD is defined as renal death, end-stage renal disease, or ESRD, or a confirmed ≥ 40% reduction in estimated glomerular filtration rate, or eGFR, which is also known as DD40. We anticipate randomizing approximately 1,600 subjects in VALOR-CKD and the trial is currently designed to terminate when the independent blinded Clinical Endpoint Adjudication Committee has positively adjudicated 511 subjects with primary endpoint events, which is anticipated to occur in the first half of 2024. The VALOR-CKD trial also includes two interim analyses for early stopping for efficacy after the accrual of 150 primary endpoint events, which is anticipated in the second half of 2021, and 250 primary endpoint events, which is anticipated in mid-2022, based on the current rate of event accrual. These interim analyses will be conducted by an independent unblinded Interim Analysis Committee. If the independent unblinded Interim Analysis Committee does not recommend stopping the trial early for efficacy, we will receive no information from these interim analyses. The VALOR-CKD trial also includes, as its first two secondary efficacy endpoints, evaluation of the effect of veverimer versus placebo after one year of treatment on patient-reported and objective measures of physical functioning, using self-reported responses to the physical function subpart of the Kidney Disease and Quality of Life Short Form, or KDQOL Physical Functioning Survey, and the Repeated Chair Stand test, respectively. Although not part of any efficacy endpoints, the VALOR-CKD trial will also provide information regarding the change from baseline in serum bicarbonate in veverimer and placebo-treated subjects.

In November 2020, Tricida revised the protocol for the VALOR-CKD trial based on feedback from the FDA in a July 2020 advice letter as well as our additional work to understand both the hazard ratio and the anticipated serum bicarbonate effect of veverimer. In collaboration with Dr. Navdeep Tangri, M.D., Ph.D. (University of Manitoba, Canada), we developed a time-dependent predictive model, or the Time-Dependent Predictive Model, in a cohort of more than 24,000 U.S. patients with metabolic acidosis and CKD. The results from this model show an 8.4% lower risk of CKD progression for each 1 mEq/L increase in serum bicarbonate. In addition, we believe the magnitude of the veverimer treatment effect in the TRCA-301/TRCA-301E trial is best described by the between-group difference in the medians, rather than the difference in the LS means, as the data are not normally distributed. The Week 52 median placebo-subtracted treatment effect in the TRCA-301E trial was an increase in serum bicarbonate of 3.15 mEq/L. Based on a median treatment effect of 3.15 mEq/L and using the Time-Dependent Predictive Model, we assume a hazard ratio of 0.76 for the VALOR-CKD trial. Based on this assumed hazard ratio, with a sample size of 1,600 subjects, the trial has 87% power to show a 24% difference in primary endpoint events. While we have not yet received comments from the FDA on the revised protocol, we believe that VALOR-CKD is adequately designed and powered to confirm the clinical benefit of veverimer treatment in slowing CKD progression.

We initiated enrollment in the VALOR-CKD trial in the fourth quarter of 2018 and have established sites throughout North America, Europe, Latin America and Asia-Pacific. As of February 22, 2021, the VALOR-CKD trial has randomized 1,433 of 1,600 subjects with an average treatment duration of approximately one year and has accrued 69 subjects with positively adjudicated primary endpoint events. In November 2020, based on feedback from the FDA, recruitment for VALOR-CKD was closed in all regions except for the United States, Canada and Western Europe. At the end of recruitment, we anticipate approximately 67% of subjects to be enrolled at Eastern European sites, 19% at U.S., Western European and Canadian sites, 7% at Latin American sites, and 7% at sites in the Asia-Pacific region. Our goal is to complete enrollment by the end of 2021; to meet this goal we may need to reopen recruitment at sites outside of the United States, but we will not reopen recruitment at sites in Eastern Europe. We intend to ensure that no single site in the VALOR-CKD trial provides ≥ 5% of the total number of trial subjects. The FDA's acceptance of the VALOR-CKD data in support of an NDA resubmission, including its assessment of the magnitude and durability of the veverimer treatment effect across the various geographical regions where the study is conducted and the acceptability of the data from non-US countries or regions which will comprise a substantial proportion of the data from the trial, will ultimately be a review issue.

We completed our Phase 3, 12-week efficacy trial, TRCA-301, and a follow-on 40-week extension trial, TRCA-301E in May 2018 and March 2019, respectively. The TRCA-301/TRCA-301E trial was designed to form the primary clinical basis for the potential approval of veverimer for the treatment for metabolic acidosis and slowing of kidney disease progression in patients with metabolic acidosis associated with CKD pursuant to the FDA's Accelerated Approval Program. The Lancet published the results of the TRCA-301 trial in March 2019 and the results of the TRCA-301E trial in June 2019.

The TRCA-301 trial was a double-blind, placebo-controlled trial that randomized 217 patients with non-dialysis dependent CKD and metabolic acidosis. The primary and secondary efficacy endpoints of the trial assessed changes in serum bicarbonate levels in veverimer-treated patients versus placebo. Chronic metabolic acidosis in CKD is characterized by a persistent serum bicarbonate level below 22 mEq/L. After 12 weeks of treatment, 59.2% of subjects in the veverimer-treated group, compared with 22.5% of subjects in the placebo group, had an increase in serum bicarbonate level of at least 4 mEq/L or achieved a serum bicarbonate level in the normal range of 22 to 29 mEq/L, which was the primary endpoint of the trial. The secondary endpoint of the trial, the least squares, or LS, mean change from baseline to week 12 in serum bicarbonate, was 4.42 mEq/L in the veverimer-treated group, compared with 1.78 mEq/L in the placebo group. The mean change in serum bicarbonate from baseline to week 12 was 4.5 mEq/L in the veverimer-treated group, compared with 1.7 mEq/L in the placebo group. The trial met both its primary and secondary endpoints in a highly statistically significant manner ($p<0.0001$ for both the primary and secondary endpoints). Veverimer was well tolerated in our TRCA-301 trial. The overall incidence of serious adverse events was low (2.3%) and balanced in the two treatment groups (2.4% TRC101; 2.2% placebo); all were assessed as not related to study drug. The only treatment emergent adverse events reported at an incidence ≥3% and ≥ 2-fold higher in the TRC101 group than in the placebo group were diarrhea (8.9% TRC101 vs. 3.2% placebo) and flatulence (4.0% TRC101 vs. 0% placebo).

The TRCA-301E trial was a blinded, 40-week extension of the 12-week TRCA-301 trial. One hundred ninety-six subjects, consisting of 114 subjects in the veverimer group and 82 subjects in the placebo group, elected and were qualified to continue in the extension trial. The primary endpoint of the TRCA-301E trial was an assessment of the long-term safety profile of veverimer versus placebo. In the veverimer group (versus placebo), we observed similar rates of treatment-emergent adverse events (81.3% versus 80.2%), fewer serious adverse events (1.8% versus 4.9%) and fewer adverse events leading to discontinuation (0% versus 1.2%). In addition, in the veverimer group (versus placebo) there were fewer subjects who discontinued study treatment (2.6% versus 9.8%) and a comparable rate of GI adverse events (21.4% versus 25.9%). After 52 weeks of treatment, 62.7% of subjects in the veverimer-treated group, compared with 37.8% of subjects in the placebo group, had an increase in serum bicarbonate level of at least 4 mEq/L or achieved a serum bicarbonate level in the normal range of 22 to 29 mEq/L, which was the first secondary endpoint of the trial ($p=0.0015$). The second secondary endpoint of the trial, the LS mean change from baseline to week 52 in serum bicarbonate, was 4.70 mEq/L in the veverimer-treated group, compared with 2.71 mEq/L in the placebo group ($p=0.0002$).

The statistical analysis plan for the TRCA-301E trial included a pre-specified safety analysis comparing the veverimer and placebo groups for the time to first occurrence of any event in the composite endpoint of all-cause mortality, dialysis/renal transplant or a confirmed ≥50% decline in eGFR, or DD50, over the combined 52-week treatment period for all subjects enrolled in the parent TRCA-301 trial. Although the trials were not designed or powered to assess this endpoint and no statistical alpha was allocated to the comparison over the combined 52-week treatment period, the annualized DD50 incidence rate was 12.0% in the placebo group versus 4.2% in the veverimer group ($p=0.0224$), which represented a 65% reduction in the annualized DD50 event rate. There were 7 confirmed eGFR reductions ≥50%, 4 deaths and 1 dialysis initiation that occurred in 10 of the 82 subjects on placebo versus 5 confirmed eGFR reductions of greater than or equal to 50%, 0 deaths and 1 dialysis initiation that occurred in 5 of the 124 subjects on veverimer.

We also assessed physical functioning both subjectively and objectively as secondary endpoints in our TRCA-301E trial. The subjective physical function endpoint examined the effect of treatment with veverimer on self-reported responses to the physical function subpart of the Kidney Disease and Quality of Life Short Form, or the KDQOL Physical Functioning Survey. This survey is a validated questionnaire for patients with kidney disease designed to assess health-related quality of life; the physical function subpart is based on activities of daily living. Subjects in the trial responded to 10 questions, each with a value of 10 points, resulting in a maximum score of 100 total points. After one year of treatment, there was no improvement in the placebo group, whose mean score decreased from a baseline score of 56 points to 55 points. However, subjects on veverimer had an 11-point improvement, on average, moving from a mean score of 53 points to 64 points ($p<0.0001$). The objective physical function endpoint examined the effect of treatment with veverimer on results of the Repeated Chair Stand Test. In this test, subjects were asked to stand up and sit down five times as quickly as possible, and the time for these five repetitions was recorded. At the end of one year of treatment, the average time for performing the Repeated Chair Stand Test decreased by 4.3 seconds on veverimer compared to 1.4 seconds on placebo compared to a baseline of 22 seconds and 21 seconds, on average, for the veverimer and placebo groups, respectively ($p<0.0001$).

We submitted our New Drug Application, or NDA, for veverimer through the Accelerated Approval Program in August 2019, and in August 2020, we received a Complete Response Letter, or CRL, from the FDA related to our NDA for veverimer. According to the CRL, the FDA is seeking additional data beyond the TRCA-301/TRCA-301E trial regarding the magnitude and durability of the treatment effect of veverimer on the surrogate marker of serum bicarbonate and expressed concern regarding whether the demonstrated effect size would be reasonably likely to predict clinical benefit. In addition, the CRL questioned the applicability of the treatment effect to the U.S. population and the practice of medicine in the United States. The FDA also expressed concern as to the reliability of the findings given that the findings for TRCA-301, and its extension, TRCA-301E, were driven by a single, high-enrolling trial site located in Eastern Europe. The CRL did not raise any concerns related to FDA's completed inspection of the highest enrolling clinical trial site in the TRCA-301/TRCA-301E trial and there was no FDA Form 483 issued. There were no safety, clinical pharmacology/biopharmaceutics, CMC, or non-clinical issues identified in the CRL. The CRL provided multiple options for resolving the identified deficiencies, including submission of the data from at least one additional adequate and well-controlled trial demonstrating the efficacy of veverimer for the treatment of metabolic acidosis associated with CKD.

We held an End-of-Review Type A meeting, or Type A meeting, with the FDA's Division of Cardiology and Nephrology, or the Division, in October 2020. The Division agreed, in principle, that an interim analysis of serum bicarbonate data from the VALOR-CKD trial proposed by Tricida could address the Division's concerns regarding the reliability of the TRCA-301/TRCA-301E trial data and the relevance of those trial findings to the U.S. population provided certain conditions were met. Based on other feedback from the FDA during the Type A meeting, we believed the Division would also require evidence of veverimer's effect on CKD progression from a near-term interim analysis of the VALOR-CKD trial for accelerated approval and that the FDA would be unlikely to rely solely on serum bicarbonate data for determination of efficacy. Accordingly, we submitted a Formal Dispute Resolution Request, or FDRR, solely requesting that the Office of New Drugs, or OND, find that the magnitude of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis associated with CKD and that it can therefore serve as the basis for accelerated approval.

In February 2021, the OND issued a decision on our FDRR. While the OND acknowledged that the TRCA-301 and TRCA-301E trials met their serum bicarbonate endpoints with statistical significance, the OND denied the appeal. In its Appeal Denied Letter, or ADL, the OND not only addressed the issue of magnitude of serum bicarbonate change, but cited all of the deficiencies in the CRL in concluding that the data provided in support of the veverimer NDA did not support approval through the Accelerated Approval Program. The OND concluded that the magnitude of the increases in serum bicarbonate levels shown in the TRCA-301/TRCA-301E trial were not of sufficient size or duration to establish that treatment with veverimer would be reasonably likely to provide a discernible reduction in CKD progression. In addition, the OND found that the intended confirmatory trial, VALOR-CKD, was underpowered to detect a 13% reduction in slowing of CKD progression. This finding was based on information included in the initial NDA submission, including the placebo-subtracted LS mean change from baseline in serum bicarbonate observed in the TRCA-301/TRCA-301E trial and the original Predictive MA Model. The OND also raised concerns regarding the robustness of the study results given that the veverimer NDA was supported by a single registrational trial (TRCA-301/TRCA-301E), which must, alone, provide persuasive evidence of benefit. Specifically, the OND noted concerns around adequate blinding, the trial results being strongly influenced by a single site, and the majority of sites for the TRCA-301/TRCA-301E trial being in Eastern Europe, where differences in patient management, including concomitant medications and diet, might affect the treatment response to veverimer and raise a concern of the applicability to a U.S. patient population. The OND also stated that, while trial results in the TRCA-301/TRCA-301E trial showed improvement in two patient-reported measures, the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test, the OND viewed this subjective data from a single trial with skepticism in the absence of data from a second trial with similar results and noted that both endpoints would require rigorous blinding to support robust conclusions. However, the OND noted that both of these changes, if eventually established by one or more additional trials, would indicate a potentially meaningful benefit of veverimer treatment—especially in CKD patients who have physical functional impairments. Separate from the ADL, we previously received feedback from the Division of Clinical Outcome Assessment, or DCOA, that reliance on these physical function endpoints for approval may require further validation.

Based on the ADL, we believe that we now have greater clarity on the potential approval of veverimer through the Accelerated Approval Program. The OND suggested that we meet with the Division to discuss submission of Week 52 serum bicarbonate results from the full randomized trial population of VALOR-CKD and that the trial should include a substantial portion of patients from the United States or from regions with "US-like" patients. If the results of this trial were to demonstrate that veverimer provides a meaningfully larger treatment effect than seen in the TRCA-301/TRCA-301E trial, then this trial, along with the results from the TRCA-301/TRCA-301E trial, could address the concerns raised in the CRL regarding the limitations and the size of the treatment response observed in the TRCA-301/TRCA-301E trial. However, whether the extent of increase in serum bicarbonate in any subsequent submission based on VALOR-CKD would support accelerated approval will remain a review issue, and will, in part, reflect the Division's assessment of the adequacy (i.e., power) of VALOR-CKD to detect the anticipated treatment effect of CKD progression in a reasonable timeframe.

Although the ADL provides greater clarity on the potential path for approval of veverimer through the Accelerated Approval Program, we believe the timeline to meet the requirements for accelerated approval as suggested in the ADL, may not result in the most rapid development path for veverimer. For example, if either of the planned interim analyses in VALOR-CKD for early stopping for efficacy results in positive renal outcomes data, this data could be available before the week 52 serum bicarbonate data from the fully enrolled VALOR-CKD trial suggested in the ADL and could serve as the basis for resubmission of the NDA. We are evaluating several options with respect to the VALOR-CKD trial that are focused on obtaining, prior to the end of 2022, additional data on the effect of veverimer on (1) CKD progression; (2) physical functioning; and (3) serum bicarbonate. We may explore the possibility of stopping the trial early for administrative reasons, which would allow analysis of the data using all alpha remaining at that time. In any event, we believe data from VALOR-CKD will be very important in furthering our understanding of the regulatory path for approval of veverimer. As such, we intend to continue the execution of the VALOR-CKD trial with consideration of both the accelerated and traditional approval pathways. Resubmission of the veverimer NDA may require additional clinical data beyond that provided by the VALOR-CKD trial.

There is a high unmet medical need for an FDA-approved chronic treatment for metabolic acidosis in patients with CKD, and a broad understanding among nephrologists that treatment of metabolic acidosis can slow CKD progression. We believe that the favorable response from nephrologists to veverimer's target product profile and the potential health and economic benefits from treating metabolic acidosis provide a significant opportunity for veverimer in the U.S. market, if approved, as the first and only FDA-approved therapy for the treatment of chronic metabolic acidosis and slowing of kidney disease progression and/or improving physical functioning in patients with metabolic acidosis and CKD.

Our Strategy

Our strategy is to develop and commercialize veverimer as the first and only FDA-approved therapy for the treatment of chronic metabolic acidosis in patients with CKD. Key elements of our strategy are to:

- Obtain FDA approval of veverimer through the Accelerated Approval Program based upon veverimer's effect on serum bicarbonate or traditional approval based upon veverimer's effect on slowing CKD progression and/or on improving physical functioning in patients with metabolic acidosis associated with CKD.

- Expand awareness of, and educate nephrologists on, the consequences of untreated metabolic acidosis in patients with CKD. We have authored and co-authored 24 and sponsored 23 peer-reviewed publications or presentations in the past two years that highlight veverimer, the serious complications of metabolic acidosis and its economic burden to the healthcare system. We have provided continuing medical education, or CME, grants related to disease awareness and treatment of metabolic acidosis and have built an educational website, MetabolicAcidosisInsights.com, for nephrologists and healthcare providers that offers resources and information related to metabolic acidosis.

- Commercialize veverimer in the United States. If veverimer is approved by the FDA, we plan to initially commercialize it in the United States by deploying an 80- to 90-person specialty sales force targeting that subset of nephrologists most focused on treating patients with CKD. With this approach, we believe we can reach a majority of the approximately 600,000 patients with metabolic acidosis and Stage 3 to 5 CKD that are cared for by nephrologists. Alternatively, we may seek to commercialize veverimer in the United States with one or more partners.

- Commercialize veverimer outside of the United States with one or more partners. We believe there is a significant commercial opportunity for veverimer in markets outside the United States. To address these markets, we plan to seek one or more partners with international sales expertise who can commercialize veverimer in target markets, if approved.

Chronic Kidney Disease and Metabolic Acidosis Represent a Major Health Crisis

Overview of CKD

CKD is a serious condition characterized by the gradual loss of essential kidney functions over time. In patients with CKD, normal fluid and electrolyte balance can no longer be maintained, and the excretion of metabolic end products, toxins and drugs is impaired. Furthermore, production and secretion of certain enzymes and hormones are disturbed.

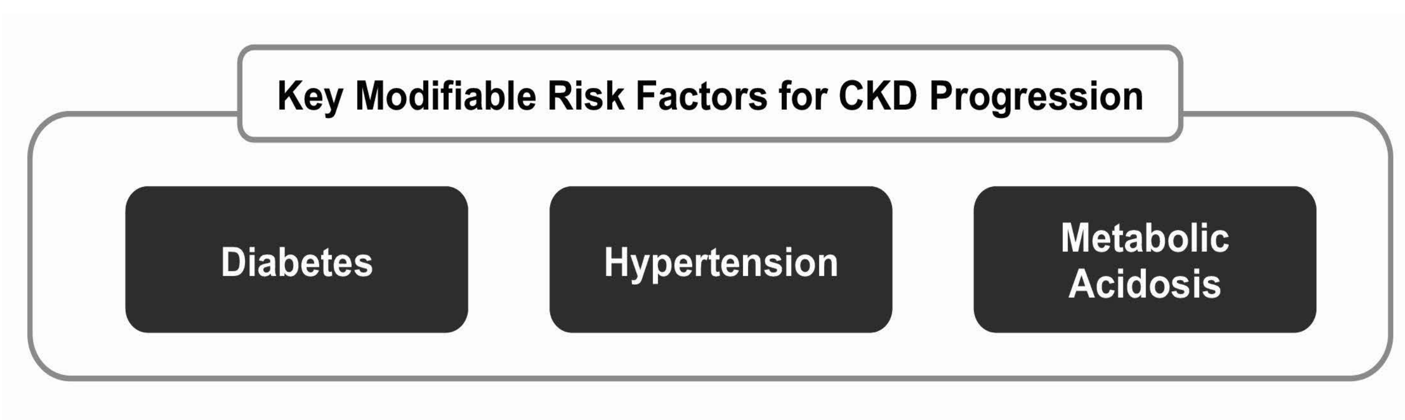
According to the Centers for Disease Control and Prevention, or CDC, more than 37 million people in the United States are afflicted with CKD, representing an overall prevalence in the adult population of approximately 15%. The incidence of CKD is primarily driven by the increasing prevalence of diabetes and hypertension. The treatment of CKD adds a tremendous financial burden to the United States, with annual Medicare expenses for CKD in 2018 totaling approximately $131.0 billion, including approximately $81.8 billion on CKD costs and approximately $49.2 billion for end-stage renal disease, or ESRD, costs. ESRD is total and permanent kidney failure that is treated with kidney dialysis or with a kidney transplant. There are approximately 775,000 people in the United States living on kidney dialysis or with a kidney transplant and approximately 130,000 new ESRD cases occur annually. Each year kidney disease kills more people than breast cancer or prostate cancer. According to the 2019 United States Renal Data System report, there were approximately 105,000 deaths from ESRD in 2018. There is a significant medical need to slow progression of kidney disease and reduce the number of patients progressing to kidney failure.

To help improve the diagnosis and management of kidney disease, the National Kidney Foundation, or NKF, has divided CKD into five stages. The severity of CKD at each stage is identified by the estimated glomerular filtration rate, or eGFR. Treatment during the first four stages of CKD focuses on ways to preserve kidney function for as long as possible. ESRD is the final stage of CKD in which the patient typically requires renal replacement therapy, i.e., dialysis or a kidney transplant, for survival.

Stages of CKD

Overview of Metabolic Acidosis

Diabetes and hypertension have long been recognized as modifiable risk factors for the progression of CKD. More recently, metabolic acidosis, a serious condition in which the body has accumulated too much acid, has also been identified as a key modifiable risk factor for the progression of CKD.

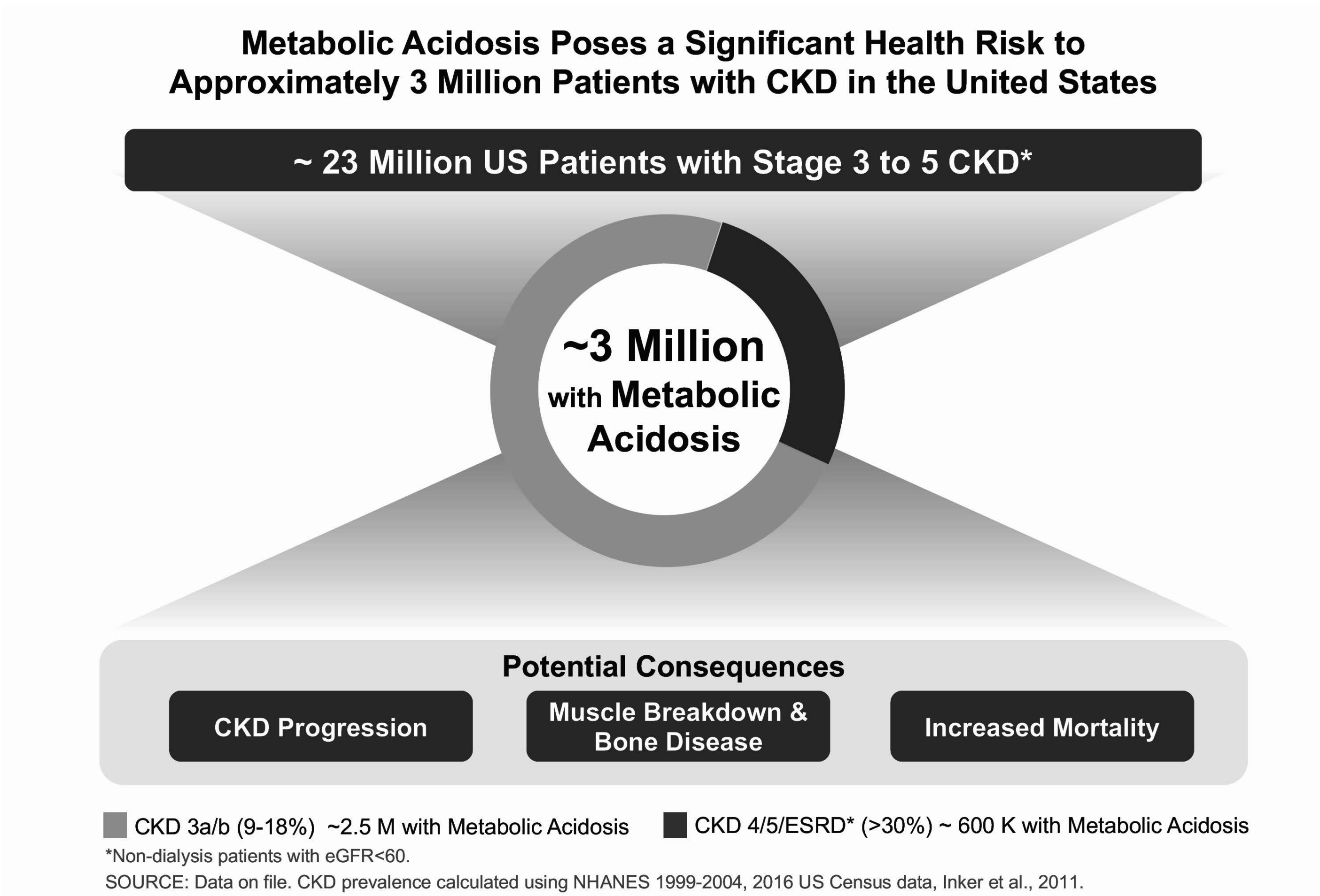


The human body generates acid every day through normal food intake and metabolism. Sources of acid include amino acids and nucleic acids from daily dietary intake and digestion of proteins. A healthy kidney counteracts these sources of acid through excretion mechanisms that rid the body of the excess acid and by restoring bicarbonate, a base that buffers acid. Metabolic acidosis results when the kidneys can no longer excrete sufficient acid or reabsorb sufficient bicarbonate back into the blood stream to balance acid production. If left untreated, metabolic acidosis can result in accelerated kidney disease progression and has also been shown to negatively impact bone and muscle health.

Metabolic acidosis can be diagnosed by measuring the level of bicarbonate in the serum, which is routinely analyzed as part of a standard metabolic panel. Properly functioning kidneys will maintain a serum bicarbonate level of between 22 to 29 milliequivalents per liter, or mEq/L. A persistent serum bicarbonate level below 22 mEq/L indicates metabolic acidosis.

The prevalence and severity of metabolic acidosis in people with CKD progressively rises as kidney function declines. We estimate the prevalence of metabolic acidosis to be 9.4% of the estimated 15 million patients with Stage 3a CKD, 18.1% of the estimated 6 million patients with Stage 3b CKD and 31.5% of the estimated 2 million patients with Stage 4 and Stage 5 CKD (non-dialysis patients), resulting in a total estimated prevalence of approximately 3 million patients with metabolic acidosis and CKD in the United States.

Metabolic Acidosis Poses a Significant Health Risk to Approximately 3 Million Patients with CKD in the United States



Metabolic acidosis can accelerate kidney disease progression and lead to bone demineralization, muscle wasting and an increased risk of mortality. In patients with CKD, adaptations by the kidneys in response to an accumulating acid load result in increased acid excretion per nephron by the remaining nephrons, but over time these adaptations have deleterious effects on kidney tissue, resulting in further kidney damage. The specific mechanisms that link metabolic acidosis to accelerated progression of kidney disease involve a cascade of events whereby acid accumulation leads to increased production of select peptides and hormones, including endothelin-1, aldosterone and angiotensin II, that increase the secretion of acid through the proximal and distal renal tubules of the remaining healthy nephrons in the compromised kidney. This provides a short-term beneficial impact on acid excretion, however, sustained over-production of these hormones results in long-term consequences, including inflammation, renal fibrosis, tubular atrophy and proteinuria. Over time, a vicious cycle of worsening metabolic acidosis and accelerated progression of kidney disease can result.

An increased risk of fractures and renal osteodystrophy as well as muscle wasting and reduced physical functioning have also been associated with worsening metabolic acidosis. In patients with CKD whose kidney function is not sufficient to excrete their daily acid load, bone and muscle provide buffers for circulating acid, resulting in loss of bone density and increased muscle protein catabolism. Two large retrospective cohort analyses found that low serum bicarbonate level was independently associated with adverse health outcomes related to physical functioning, such as gait speed, quadriceps strength, failure to thrive and fractures/falls (Abramowitz et al., 2011; Reaven et al., 2019). Several prospective studies of patients with metabolic acidosis and CKD have reported that treatment of metabolic acidosis can increase muscle mass (de Brito-Ashurst et al., 2009; Dubey et al., 2018), improve muscle function (Abramowitz et al., 2013) and physical function related quality of life (de Brito-Ashurst et al., 2015).

The importance of treating metabolic acidosis has been noted in both National and International kidney disease treatment guidelines. The NKF's Kidney Disease Outcomes Quality Initiative, or KDOQI, guidelines and the International Society of Nephology's Kidney Disease: Improving Global Outcomes, or KDIGO, guidelines suggest that in patients with CKD, serum bicarbonate be maintained above 22 mEq/L. Serum bicarbonate concentrations <22 mEq/L are associated with increased risk of CKD progression and increased risk of death.

There is Evidence that Low Serum Bicarbonate Levels are Associated with Increased Risk of CKD Progression and that Treating Metabolic Acidosis Can Slow the Progression of CKD

We believe several prospective clinical studies have shown that treating metabolic acidosis can slow the progression of CKD, and that multiple retrospective studies provide qualitative and quantitative evidence for the relationship between metabolic acidosis and the risk of progression of CKD across a wide range of baseline eGFRs and serum bicarbonate levels.

In particular, five prospective trials (Garneata et al., 2016; de Brito-Ashurst et al., 2009; Phisitkul et al., 2010; Dubey et al., 2018; Di Iorio et al., 2019) studying patients with Stage 3 to 5 CKD and metabolic acidosis demonstrated slowing of CKD progression following an increase in serum bicarbonate with three different interventions, comprising a very low-protein diet, oral sodium bicarbonate and oral sodium citrate. Increases in serum bicarbonate resulted in improved clinical outcomes, including fewer patients who progressed to ESRD and/or experienced significant declines of eGFR. Additionally, clinical trials reported by Goraya et al., 2013 and 2014 and Mahajan et al., 2010 showed that, in patients with Stages 2 to 4 CKD due to hypertensive nephropathy, increasing serum bicarbonate levels with sodium bicarbonate or a low protein diet rich in fruits and vegetables resulted in reduced markers of kidney injury and slower decline in eGFR. It should be noted that these trials were open-label trials that generally did not enroll patients with diabetes, heart failure, edema, uncontrolled hypertension, obesity, clinical evidence of cardiovascular disease, and other conditions related to sodium sensitive comorbidities. As such, the patients in these trials did not fully represent the general population of patients with metabolic acidosis and CKD. It is estimated that approximately 90% of late stage patients with CKD have sodium sensitive comorbidities.

Four large, published retrospective database analyses show an association between higher serum bicarbonate levels and slower progression of CKD, independent of baseline eGFR and other factors such as age, sex, proteinuria, hypertension and diabetes (Dobre et al., 2013; Raphael et al., 2011; Shah et al., 2009; Tangri et al., 2011). In these four distinct large cohorts of patients with CKD, the analyses all demonstrate that clinical outcomes for patients with CKD with serum bicarbonate levels that are below normal (i.e., <22 mEq/L) are significantly worse compared to patients with normal serum bicarbonate levels (i.e., 22 to 29 mEq/L).

The Unmet Medical Need for the Chronic Treatment of Metabolic Acidosis

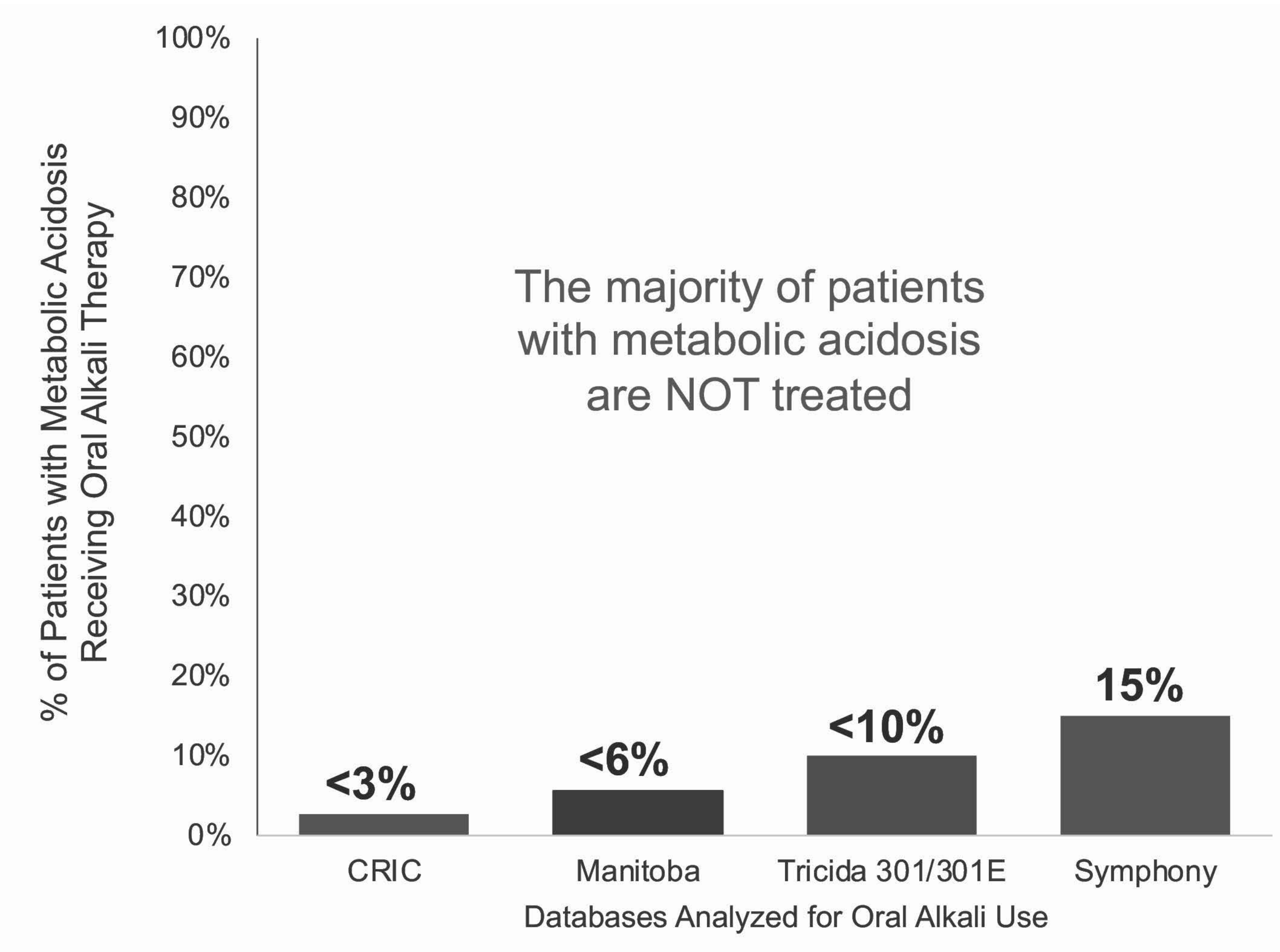
Currently, there are no FDA-approved therapies for the chronic treatment of metabolic acidosis. Kidney disease treatment guidelines suggest treating metabolic acidosis when serum bicarbonate falls below 22 mEq/L, but in the absence of an FDA-approved treatment, physicians are left with recommending either protein-restricted diets to reduce acid intake or unapproved, over-the-counter supplements that have not undergone the scrutiny of rigorous clinical examination, including evaluation of safety, efficacy and their interactions with other drugs.

Several analyses of retrospective databases show that, despite its prevalence, metabolic acidosis has gone largely untreated. One recent analysis of the diagnosis and treatment rates of metabolic acidosis in patients with CKD indicates that it is both underdiagnosed and undertreated. At the ASN Kidney Week 2019 Meeting, Dr. Tangri, presented an analysis of data from the Symphony Health Solutions Integrated Dataverse®, or IDV, which quantified the diagnosis and treatment rates of metabolic acidosis in patients with CKD. This analysis, which was derived from a cohort of approximately 87,000 patients, showed that only 21% of patients with confirmed laboratory evidence of metabolic acidosis and CKD had been diagnosed with metabolic acidosis and only 15% of these patients had been treated for metabolic acidosis.

Three other analyses indicate that oral alkali supplements are used in less than 10% of patients with metabolic acidosis and CKD. An evaluation of data from the Chronic Renal Insufficiency Cohort, or CRIC, study (Dobre et al.,

2012) showed that less than 3%, or 28 of 1,039 patients with CKD and serum bicarbonate levels ≤22mEq/L were receiving an oral alkali supplement. A retrospective cohort study of adults in Manitoba, Canada, (Tangri et al., 2020), concluded that less than 6% of 5,368 patients with CKD and serum bicarbonate values between 12-22 mEq/L were receiving an oral alkali supplement. Because the Canadian health care system includes oral alkali supplements in their formulary, the analysis included an evaluation of the adherence to oral alkali supplements. The data show that, more than two thirds of patients (68%) had discontinued oral alkali therapy at one year. The use of oral alkali supplements in patients with metabolic acidosis and CKD who were enrolled in the TRCA-301/TRCA-301E clinical trial was less than 10% of subjects enrolled in the study (Wesson et al., 2019).

Oral Alkali Use is Low in Patients with Metabolic Acidosis and CKD



Dobre, 2012, Tangri 2020, Wesson, 2019, Tangri 2019.

Our primary research indicates that most nephrologists understand the importance of treating metabolic acidosis to slow kidney disease progression, yet the analyses of actual treatment rates indicate a serious gap between the understanding and actual diagnosis and treatment. We believe that this gap is due to the lack of an FDA-approved chronic treatment for metabolic acidosis that can be used in the broad population of patients with metabolic acidosis and CKD, including those with sodium-sensitive comorbidities.

The low use of oral alkali supplements may be explained by the lack of supportive data from blinded, randomized, placebo-controlled clinical trials that confirm the efficacy and safety of these unapproved supplements. While clinical research studies conducted in carefully selected patient populations have shown that oral alkali supplementation can result in slowing of CKD progression in patients with metabolic acidosis, two recent multicenter, placebo-controlled studies that used doses of sodium bicarbonate typically used in clinical practice, i.e., 0.5 to 1.0 grams, three times daily, both achieved very little difference in mean serum bicarbonate level between the active and placebo groups (approximately 1 mEq/L difference after 2 years) and showed no clinical benefits of sodium bicarbonate treatment (the BiCARB Study, Witham et al., ERA-EDTA Poster Presentation 2019; Melamed et al., 2019). The doses of sodium bicarbonate used in these trials may not have been large enough to achieve sufficient separation in serum bicarbonate in active- versus placebo-treated subjects. These doses may have been chosen because of concern for the deleterious effect of sodium that is delivered with orally administered alkali supplements, particularly in the CKD patient population. Each gram of sodium bicarbonate delivers 274 mg of sodium.

Approximately 90% of patients with later-stage CKD suffer from sodium-sensitive comorbid conditions, such as hypertension, cardiovascular disease, heart failure or edema, and require a sodium-restricted diet. KDIGO guidelines recommend that patients with CKD consume less than 2 grams of total sodium per day, but according to the CDC, the average diet in the United States includes approximately 3.4 grams of sodium each day. It has been demonstrated that achieving a 2 to 3 mEq/L increase in serum bicarbonate requires 4 to 6 grams of sodium bicarbonate (for an 80 kilogram, or kg, patient) which results in an additional 1.1 to 1.6 grams of sodium added to the patient's daily intake, which is already in excess of guideline recommendations (Abramowitz et al., 2013).

The effects of oral alkali supplementation on overall health and wellbeing also require further evaluation. One of the first multicenter, randomized, double-blind, placebo-controlled trials of oral sodium bicarbonate versus placebo (Witham et al., ERA-EDTA Poster Presentation 2019) was commissioned by the UK National Institute for Health Research (NIHR) Health Technology Assessment Programme to evaluate the clinical and cost-effectiveness of oral sodium bicarbonate in the management of older people with CKD and mild metabolic acidosis. The trial enrolled 300 non-dialysis patients with Stage 4 or 5 CKD with serum bicarbonate concentrations <22 mEq/L recruited from 27 sites in the United Kingdom. Subjects were randomized to treatment with approximately 1.5 to 3 grams of sodium bicarbonate per day or placebo. The primary outcome and additional outcome measures were designed to assess physical function improvements and health related quality of life measures. Following 12 months of treatment, there was no significant treatment effect for the primary outcome of the between-group difference in the Short Physical Performance Battery at 12 months (-0.4 points; 95% CI -0.9 to 0.1, p=0.15). There was no significant treatment benefit seen for any of the secondary outcomes. Adverse events were more frequent in the sodium bicarbonate arm (457 versus 400) and the time to commencing renal replacement therapy was similar in both groups (HR 1.22, 95% CI 0.74 to 2.02, p=0.43). Sodium bicarbonate provided no significant treatment effect and adverse events were more frequent in the bicarbonate arm. Health economic analysis showed lower quality of life and higher costs in the sodium bicarbonate arm at one year. In addition, placebo dominated sodium bicarbonate for all sensitivity analyses of incremental cost-effectiveness. The discontinuation rates in the BICARB trial were 25% and 30% at Year 1 in the sodium bicarbonate group and placebo group, respectively, and 47% and 46% at Year 2 in the sodium bicarbonate group and placebo group, respectively.

Effects of sodium bicarbonate treatment on GI tolerability, blood pressure and volume status have been observed in some clinical trials. For example, in a randomized, placebo-controlled, open-label single-site study conducted by Dubey et al., 2018, six months of treatment with sodium bicarbonate was less well tolerated than placebo. This study evaluated a broader population of patients with metabolic acidosis and CKD, including those with sodium-sensitive comorbidities. Overall, adverse events occurred in significantly (p=0.01) more subjects in the sodium bicarbonate group compared to the control group. The safety profile of oral sodium bicarbonate showed that more subjects experienced GI side effects, fluid retention and worsening hypertension compared to placebo, despite significantly higher use of diuretics in the sodium bicarbonate group (p=0.008).

The use of sodium-based alkali supplements may also impact the effectiveness of other medications important to the treatment of many patients with CKD. In particular, renin-angiotensin-aldosterone-system inhibitors, or RAASi, are one of the only classes of agents that have been proven to slow CKD progression. Higher sodium intake has been associated with significant reductions in the effectiveness of these agents. A study by Lambers Heerspink and colleagues (Lambers Heerspink et al., 2012) evaluated the impact of low, medium and high levels of 24-hour sodium/creatinine ratio in patients administered angiotensin II receptor blockers, or ARBs, versus non-RAASi treated patients. They concluded that "The renal and cardiovascular protective effects of ARB therapy compared with non-RAASi-based therapy attenuated in subjects with larger consumption of sodium so that in subjects with the highest sodium intake the treatment effects on hard renal and cardiovascular outcomes were completely annihilated." Approximately 70% of patients with CKD are treated with RAASi to manage their hypertension.

Given the lack of a proven safe and efficacious agent to effectively raise serum bicarbonate and treat metabolic acidosis, we believe there is a significant unmet medical need for an FDA-approved agent to chronically treat metabolic acidosis in the approximately 3 million patients in the United States that are afflicted with metabolic acidosis and CKD.

Our Solution—Veverimer

Veverimer is a novel, non-absorbed, orally-administered polymer that is designed to bind hydrochloric acid in the GI tract and remove it from the body through excretion in the feces, thereby decreasing the total amount of acid in the body and increasing serum bicarbonate. Veverimer is administered orally as a suspension in water. Veverimer removes acid from the GI tract without delivering additional sodium or other counterions, such as potassium or calcium, which, if approved, would allow for the chronic treatment of patients with common sodium-sensitive comorbidities such as hypertension, edema and heart failure.

Veverimer Target Product Profile

We have designed veverimer to target the following product profile:

- Effectively Treat Metabolic Acidosis: Bind and remove sufficient amounts of acid such that a majority of the patients will achieve a clinically meaningful increase in serum bicarbonate. Subject to the results of our renal outcomes trial, VALOR-CKD, veverimer may also slow the progression of CKD through the treatment of metabolic acidosis.

- Well-Tolerated: Based on our long-term TRCA-301E trial results, patients reported GI-related adverse events at a similar rate to placebo. These events were generally mild, self-limited and did not require dose adjustment of veverimer.

- Suitable for a Broad Population of Patients, including Patients with Sodium-Sensitive Comorbidities: Treat metabolic acidosis without delivering sodium or other counterions.

- Compatible with Other Medications: Allow concomitant dosing of common CKD medications. Veverimer's unique characteristics include a particle size designed to prevent systemic absorption and size-exclusion that provides high selectivity for hydrochloric acid.

- Convenient, Once-Daily, Oral Administration: In our TRCA-301/TRCA-301E trial, subjects self-administered 3-, 6- or 9-gram doses, once daily, with high overall compliance.

- Room-Temperature Stable: Current data demonstrate 12-month room temperature stability and we plan to have data supporting 24-month shelf-life at room temperature at the time of the commercial launch.

Veverimer Mechanism of Action

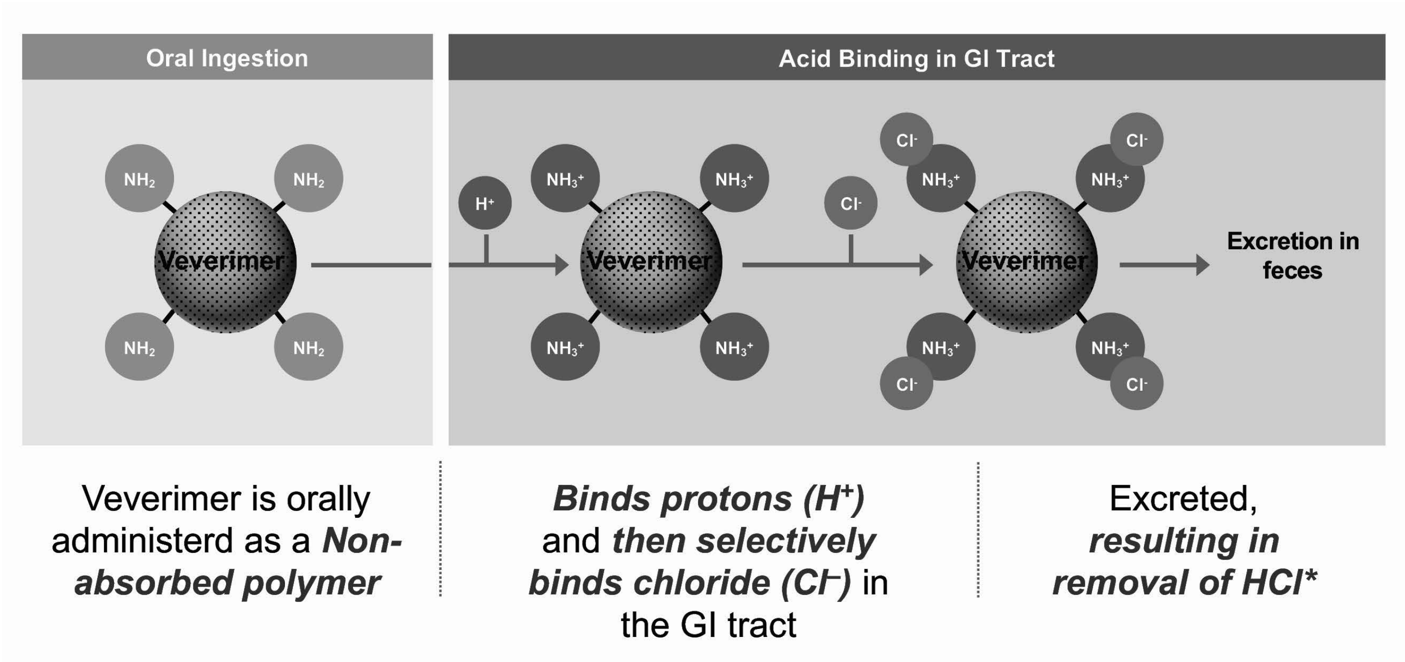
The human body generates acid every day through normal food intake and metabolism. Sources of acid include amino acids and nucleic acids from daily dietary intake and digestion of proteins. The daily load of nonvolatile acids from metabolic processes amounts to approximately 1 mEq per kg of body weight, or 50 to 100 mEq per day for adults. Prior studies with alkali supplementation have shown that neutralization of 40% to 80% (20 to 80 mEq) of the daily acid produced can increase serum bicarbonate levels (de Brito-Ashurst et al., 2009; Phisitkul et al., 2010).

Acid binding in the GI tract is a novel approach to treating metabolic acidosis and increasing serum bicarbonate levels without introducing deleterious counterions or metals. This approach mimics the physiologic response to acid removal seen with persistent vomiting or nasogastric suction that results in an elevated serum bicarbonate level. To achieve the desired effect of increasing serum bicarbonate with a convenient daily dose of less than 10 grams per day, an acid binding polymer should have an amine capacity to bind at least 5 mEq of proton/gram. Once protonated, the acid binding polymer needs to preserve the effect of the proton binding by not removing anions such as fatty and bile acids that represent precursors metabolized to bicarbonate in the blood. The complementary anion to be bound that ensures net acid removal from the GI tract is chloride, the smallest anion present in the GI tract.

Veverimer is a low-swelling, spherical polymer bead that is approximately 100 micrometers in diameter. It is a single, high molecular weight, crosslinked polyamine molecule. The size of veverimer prevents systemic absorption from the GI tract. The high degree of cross-linking within veverimer limits swelling and the overall volume in the GI tract, with the goal of facilitating good GI tolerability. The high amine content of veverimer provides proton binding capacity of approximately 10 mEq/gram of polymer. Size exclusion built into the three-dimensional structure of the polymer enables preferential binding of chloride versus larger inorganic and organic anions, including phosphate, citrate, fatty acids and bile acids. This size exclusion mechanism allows a majority of the binding capacity to be used for hydrochloric acid binding.

The mechanism of action of veverimer is illustrated below:

Veverimer Mechanism of Action



Our Development Program for Veverimer

Overview

The key clinical trials in our development program for veverimer include our ongoing VALOR-CKD trial, a completed 135-subject, Phase 1/2 trial, TRCA-101, a completed 217-subject, Phase 3 clinical trial, TRCA-301 and a completed 196-subject, Phase 3 extension trial, TRCA-301E.

Our VALOR-CKD trial is evaluating the efficacy and safety of veverimer in delaying CKD progression and whether treatment with veverimer improves physical functioning in subjects with metabolic acidosis. The primary endpoint in VALOR-CKD is a composite of renal death, end-stage renal disease (ESRD) or a confirmed ≥ 40% reduction in estimated glomerular filtration rate (eGFR) (DD40). We anticipate randomizing approximately 1,600 subjects in VALOR-CKD and the trial is currently designed to terminate when 511 subjects with primary endpoint events have been positively adjudicated. The VALOR-CKD trial also includes two interim analyses for early stopping for efficacy: after 150 primary endpoint events and 250 primary endpoint events have accrued. The VALOR-CKD trial also includes, as its first two secondary efficacy endpoints, evaluation of the effect of veverimer versus placebo after one year of treatment on patient-reported and objective measures of physical functioning, using the KDQOL Physical Functioning Survey and the Repeated Chair Stand test, respectively. Although not part of any efficacy endpoints, the VALOR-CKD trial will also provide information regarding the change from baseline in serum bicarbonate in veverimer and placebo-treated subjects.

Both TRCA-101 and TRCA-301 utilized change from baseline in serum bicarbonate as their primary endpoint. Eligible subjects who completed the 12-week treatment period in the TRCA-301 trial were invited to continue in our extension trial, TRCA-301E. The primary endpoint of the TRCA-301E trial was the assessment of the long-term safety profile of veverimer versus placebo.

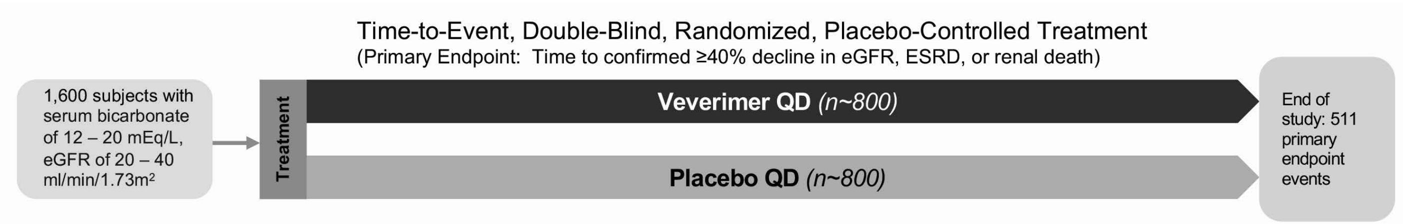
Veverimer Clinical and Nonclinical Programs

VALOR-CKD Renal Outcomes Trial

The protocol for the VALOR-CKD trial was designed in collaboration with a Steering Committee of international key opinion leaders in the fields of chronic kidney disease progression and metabolic acidosis and with input from the FDA. It is a multicenter, randomized, double-blind, placebo-controlled trial of subjects with Stage 3b or 4 CKD (eGFR of 20 to 40 mL/min/1.73m^2) and metabolic acidosis (serum bicarbonate levels of 12 to 20 mEq/L). The eligibility criteria for the

VALOR-CKD trial are similar to those used in our TRCA-301 trial. Based on observations from the TRCA-301 trial, we strengthened the screening requirements in the VALOR-CKD trial to enable enrollment of subjects with confirmed metabolic acidosis at baseline. In the VALOR-CKD trial, subjects are treated with veverimer (3, 6 or 9 g QD) or placebo, with titration to attempt to maintain serum bicarbonate in the normal range (22 to 29 mEq/L).

VALOR-CKD Renal Outcomes Trial



The primary endpoint of the VALOR-CKD trial compares the time to first renal event, with a renal event defined as a confirmed ≥ 40% reduction in eGFR, progressing to ESRD, or renal death, in veverimer-treated subjects versus subjects in the placebo group. We anticipate randomizing approximately 1,600 subjects and the trial is designed to end when the independent blinded Clinical Endpoint Adjudication Committee has positively adjudicated 511 subjects with primary endpoint events, which , based on the current rate of event accrual, we estimate will occur in the first half of 2024. The VALOR-CKD trial also includes two interim analyses for early stopping for efficacy: after 150 subjects have accrued primary endpoint events (anticipated in the second half of 2021, based on the current rate of event accrual) and after 250 subjects have accrued primary endpoint events (anticipated in mid-2022, based on the current rate of event accrual). These interim analyses will be conducted by an independent unblinded Interim Analysis Committee. If the independent unblinded Interim Analysis Committee does not recommend stopping the trial early for efficacy, we will receive no information from these interim analyses. The interim analyses employ the O'Brien-Fleming alpha spending function, which preserves the majority of alpha for the final analysis when the trial reaches 511 subjects with primary endpoint events. The VALOR-CKD trial also includes, as its first two secondary efficacy endpoints, evaluation of the effect of veverimer versus placebo after one year of treatment on patient-reported and objective measures of physical functioning, using the KDQOL Physical Functioning Survey and the Repeated Chair Stand test, respectively. Although not part of any efficacy endpoints, the VALOR-CKD trial will also provide information regarding the change from baseline in serum bicarbonate in veverimer and placebo-treated subjects.

In order to appropriately power the VALOR-CKD trial, we worked with Dr. Navdeep Tangri to determine the anticipated magnitude of impact from each 1 mEq/L increase in serum bicarbonate on kidney disease progression. Dr. Tangri is an Associate Professor of Medicine in the Department of Medicine and Community Health Sciences and the Scientific Director of the Chronic Disease Innovation Center at University of Manitoba. He is a recognized expert in CKD risk prediction and has developed a validated model which is an accepted standard for predicting the risk of kidney disease progression which was published in The Journal of the American Medical Association, or JAMA (Tangri et al., 2011). Initially, Dr. Tangri developed for us a predictive metabolic acidosis model, or the Predictive MA Model, that specifically looked at the quantitative relationship between serum bicarbonate level and the risk of kidney disease progression. The relationship between serum bicarbonate and the risk of a ≥ 40% decline in eGFR or ESRD was approximately linear, independent of baseline kidney function (eGFR), and consistent across subgroups of patients with reduced eGFR and those with established metabolic acidosis. Furthermore, it showed that each 1 mEq/L increase in serum bicarbonate was associated with a 6% to 9% reduction in the risk of CKD progression. These data were reviewed with the FDA and formed the basis for our original powering assumptions for the VALOR-CKD trial as submitted in the initial NDA.

After submission of the NDA, we developed with Dr. Tangri a time-dependent predictive model, or the Time-Dependent Predictive Model, that used all available measurements of serum bicarbonate collected longitudinally in a cohort of 24,384 U.S. participants with CKD Stages 3-5 and metabolic acidosis from the Optum® EHR+ Integrated database, who had an average of 19 measurements of serum bicarbonate over a median follow up time of 3.7 years (interquartile range: 1.6-5.9 years). This model assessed the quantitative relationship between within-patient change in serum bicarbonate and the risk of a ≥ 40% decline in eGFR or ESRD. The results from this new Time-Dependent Predictive Model are consistent with those of our previous model and show an 8.4% lower risk of CKD progression for each 1 mEq/L higher serum bicarbonate.

In addition, as we continued to analyze data from our completed TRCA-301/TRCA-301E trial, we learned that the magnitude of the veverimer treatment effect in those studies is best described by the between-group difference in the medians, rather than the difference in the LS means as originally specified, because the data are not normally distributed. The Week 52 median placebo-subtracted treatment effect in the TRCA-301E trial was an increase in serum bicarbonate of 3.15 mEq/L.

Using the 8.4% reduction in the risk of CKD progression per 1 mEq/L increase in serum bicarbonate from the Time-Dependent Predictive Model and a median treatment effect of 3.15 mEq/L, we assume a hazard ratio of 0.76 for the VALOR-CKD trial. Based on this assumed hazard ratio, with a sample size of 1,600 subjects, the trial has 87% power to show a 24% difference in primary endpoint events. Based on this analysis, which was completed after receipt of the CRL from the FDA, we believe that the VALOR-CKD trial is adequately designed and powered to confirm the clinical benefit of veverimer treatment in slowing CKD progression.

The VALOR-CKD trial also includes, as its first two secondary efficacy endpoints, evaluation of the effect of veverimer versus placebo after one year of treatment on patient-reported and objective measures of physical functioning, using the KDQOL Physical Functioning Survey and the Repeated Chair Stand test, respectively. Although not part of any efficacy endpoints, the VALOR-CKD trial can also provide information regarding the change from baseline in serum bicarbonate in veverimer and placebo-treated subjects.

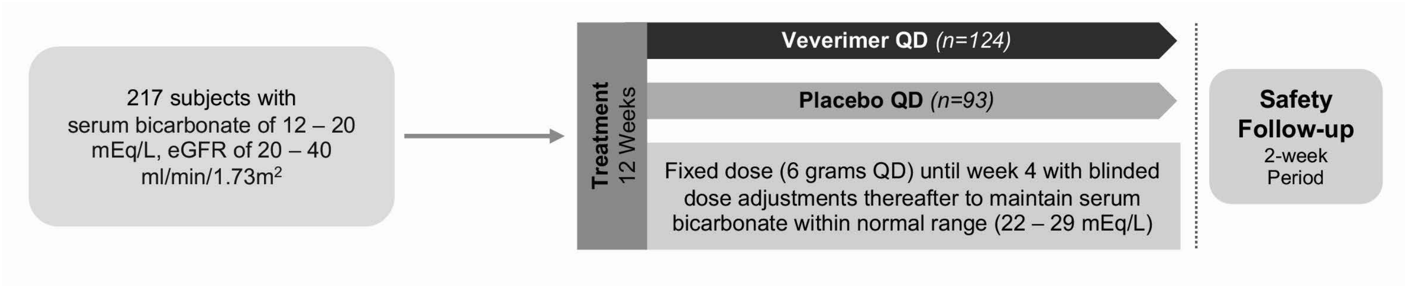
As of February 22, 2021, the VALOR-CKD trial has randomized 1,433 of 1,600 subjects with an average treatment duration of approximately one year and has accrued 69 of the 511 required subjects with positively adjudicated primary endpoint events. Based on feedback from the FDA at the End-of-Review Type A meeting, recruitment has been closed in all regions except for the United States, Canada and Western Europe. At the end of recruitment, we anticipate approximately 67% of subjects to be enrolled at Eastern European sites, 19% at U.S., Western European and Canadian sites, 7% at Latin American sites, and 7% at sites in the Asia-Pacific region. Our goal is to complete enrollment by the end of 2021; to meet this goal we may need to reopen recruitment at sites outside of the United States, but we will not reopen recruitment at sites in Eastern Europe. We intend to ensure that no single site in the VALOR-CKD trial provides ≥ 5% of the total number of trial subjects. The FDA's acceptance of the VALOR-CKD data in support of an NDA resubmission, including its assessment of the magnitude and durability of the veverimer treatment effect across the various geographical regions where the study is conducted and the acceptability of the data from non-US countries or regions which will comprise a substantial proportion of the data from the trial, will ultimately be a review issue.

TRCA-301 Phase 3 Clinical Trial and TRCA-301E Extension Clinical Trial

TRCA-301 Phase 3 Clinical Trial

In May 2018, we completed our Phase 3 clinical trial, TRCA-301. We conducted the trial at 47 sites in the United States and Europe, of which 37 sites enrolled patients. In the TRCA-301 trial, 190 trial subjects were located in Eastern Europe, and 27 trial subjects were located in the U.S. In March 2019, the results of this trial were published in The Lancet. The double blind, randomized, placebo-controlled trial enrolled 217 subjects with Stage 3b or 4 CKD (an estimated glomerular filtration rate, or eGFR, of 20 to 40 mL/min/1.73m^2) and low serum bicarbonate levels (between 12 and 20 mEq/L). At the beginning of the 12-week treatment period, subjects were randomized in a 4:3 ratio to receive once-daily, or QD, veverimer or placebo. Subjects in the active group initially received a QD dose of 6 grams of veverimer (2 packets). After week 4, bi-directional blinded dose adjustments to 3 grams/day (1 packet) or 9 grams/day (3 packets) were allowed in order to attempt to maintain serum bicarbonate in the normal range. Subjects in the placebo group initially received 2 packets of placebo, with the same ability for bi-directional dose adjustments after 4 weeks. The dose titration algorithm required down-titration at serum bicarbonate values of ≥ 27 to ≤ 30 mEq/L. Subjects with a serum bicarbonate level >30 mEq/L underwent an interruption of the study drug in accordance with the titration algorithm. Subjects were permitted to continue their existing oral alkali supplement during the trial, provided dosing remained stable. Because the appearance and weight of veverimer and placebo were not identical, study drug dispensing, preparation, supervision of the subject's first dose in the clinic, and study drug accountability were done by an unblinded designated site staff member who had no other responsibilities for the trial. The trial sponsor, statistician, investigators, patients, and all CRO staff (except personnel responsible for monitoring drug dispensing and accountability records) remained blinded to treatment assignments throughout the trial. Site personnel were trained on blinding requirements, and these requirements were detailed in a blinding plan.

TRCA-301 Phase 3 Clinical Trial



The underlying comorbid conditions of veverimer-treated subjects and subjects in the placebo group in the TRCA-301 trial were well-balanced and included 97% hypertension, 65% type 2 diabetes, 44% left ventricular hypertrophy, and 31% congestive heart failure. During the three months prior to baseline, 12% of subjects had shortness of breath with exertion and 9% had edema or fluid overload. Nine percent of the total patient population in the trial reported the use of oral alkali therapy at baseline.

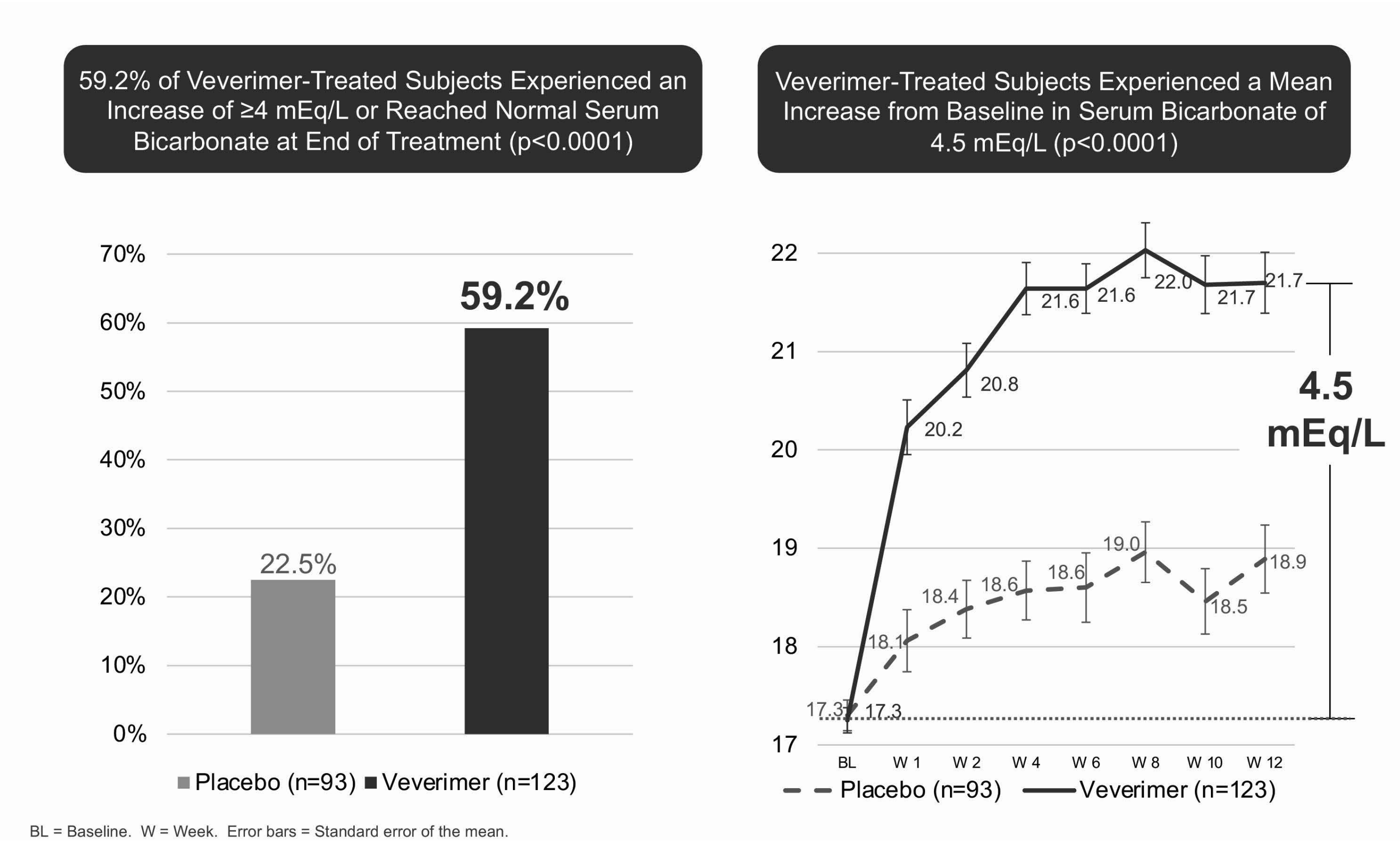
TRCA-301 Phase 3 Trial Results

Primary and Secondary Endpoints

The serum bicarbonate levels of subjects were measured on day 1, week 1, week 2, and bi-weekly thereafter, up to and including week 14, which was a final post-treatment visit for those subjects not continuing into the TRCA-301E extension trial. The primary endpoint of the trial was an increase in serum bicarbonate level of at least 4 mEq/L or achieving a serum bicarbonate level in the normal range of 22 to 29 mEq/L, at the end of the 12-week treatment period. The secondary endpoint of the trial was the change from baseline in serum bicarbonate at the end of the 12-week treatment period.

Analysis of our TRCA-301 Phase 3 trial demonstrated that treatment with veverimer resulted in statistically significant increases in serum bicarbonate, meeting both the primary and secondary endpoints. After 12 weeks of treatment, 59.2% of subjects in the veverimer-treated group, compared with 22.5% of subjects in the placebo group, had an increase in serum bicarbonate level of at least 4 mEq/L or achieved a serum bicarbonate level in the normal range of 22 to 29 mEq/L, which was the primary endpoint of the trial. The secondary endpoint of the trial, the least squares, or LS, mean change from baseline to week 12 in serum bicarbonate, was 4.42 mEq/L in the veverimer-treated group, compared with 1.78 mEq/L in the placebo group. The mean change in serum bicarbonate from baseline to week 12 was 4.5 mEq/L in the veverimer-treated group, compared with 1.7 mEq/L in the placebo group. The results of the primary and secondary endpoints were both highly statistically significant ($p<0.0001$).

Summary Data for Our Phase 3 Clinical Trial, TRCA-301



Safety

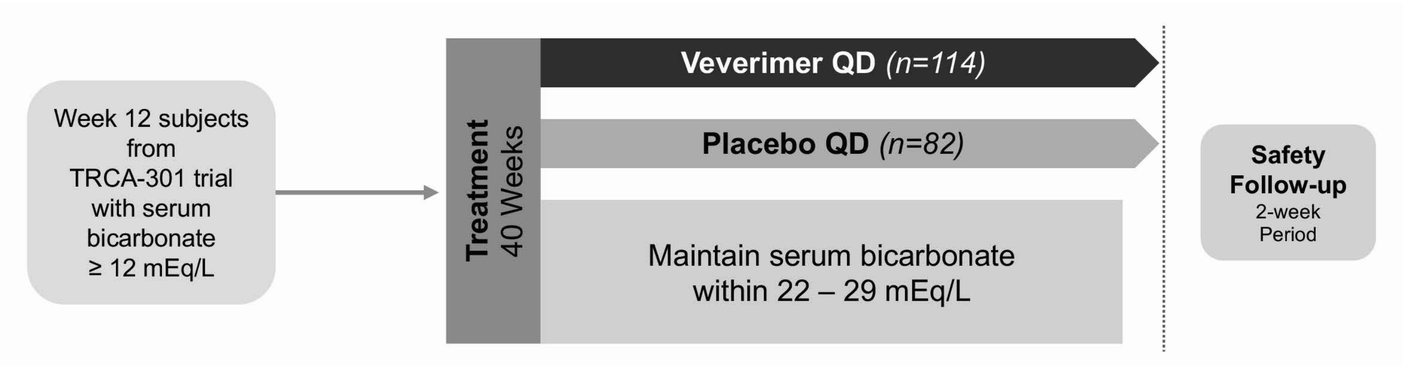
The overall safety profile of veverimer observed in our Phase 3 trial, TRCA-301, is consistent with that expected for the general population of patients with Stage 3 to 5 non-dialysis CKD and with similar non-absorbed polymer drugs with a site of action in the gastrointestinal tract. The incidence of serious adverse events was low and balanced in the two treatment groups. The types of serious adverse events were consistent with those expected in the study population, and none of the serious adverse events were assessed to be related to treatment by the trial investigator, Medical Monitor or Drug Safety and Pharmacovigilance Team. There were two deaths in the trial, and both of these occurred in the placebo group.

Veverimer was well tolerated in our Phase 3 trial, TRCA-301. In total, over 95% of subjects in each of the groups completed the trial. Overall treatment-related adverse events occurred in 9.7% of subjects in the placebo group and 13.7% of veverimer-treated subjects. The most common treatment-related adverse events were mild to moderate GI disorders, which occurred in 5.4% of subjects in the placebo group and 12.9% of veverimer-treated subjects. The treatment-related GI adverse events that occurred in more than one subject in the trial included diarrhea, flatulence, nausea and constipation. The only other treatment-related adverse event that occurred in more than one subject was paresthesia (1.1% of subjects in the placebo group and 0.8% of veverimer-treated subjects). There were no apparent effects of veverimer on serum parameters, such as sodium, calcium, potassium, phosphate, magnesium, or low-density lipoprotein observed in the trial that would indicate off-target effects of veverimer. A high serum bicarbonate level, defined as greater than 30 mEq/L, was observed transiently in 2 subjects, or 0.9%. Discontinuation of veverimer per the protocol-defined dosing algorithm resulted in normalization of serum bicarbonate in these subjects.

TRCA-301E Extension Trial

The TRCA-301E trial was a blinded, 40-week extension of the 12-week TRCA-301 trial, which randomized 217 subjects with non-dialysis dependent CKD and metabolic acidosis to treatment with veverimer (N=124) or placebo (N=93). Two hundred eight (208; 95.9%) subjects completed the 12-week treatment period in the TRCA-301 trial and had the option to continue into the extension trial and receive the same blinded treatment (veverimer or placebo) to which they were assigned in the parent study. Of these, one hundred ninety-six subjects (196; 94.2%), (114 in the veverimer group and 82 in the placebo group) elected and were qualified to continue in the extension trial. One hundred eleven (111; 97.4%) subjects in the veverimer group and 74 (90.2%) subjects in placebo group completed the one-year treatment period. In the TRCA-301E trial, 179 of the enrolled trial subjects were located in Eastern Europe and 17 of the enrolled trial subjects were located in the U.S.

TRCA-301E Phase 3 Extension Clinical Trial



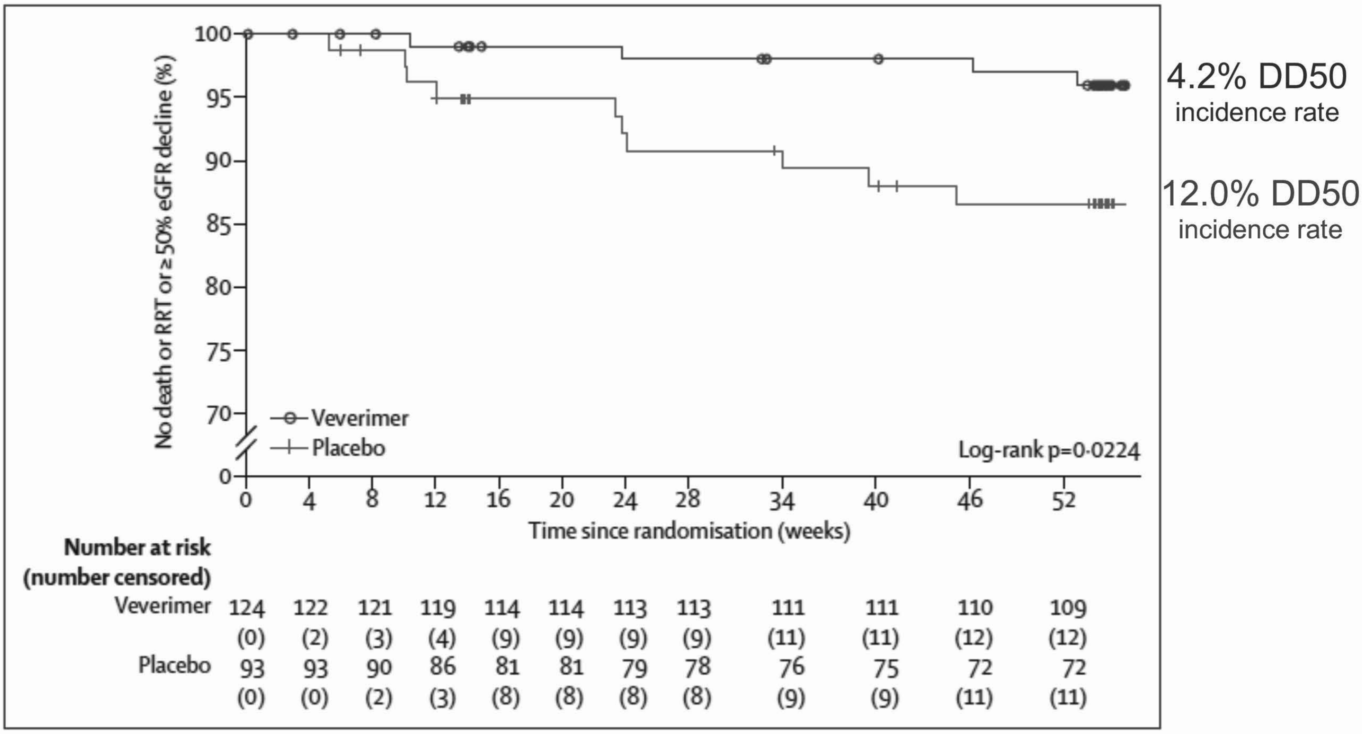
TRCA-301E Clinical Trial Results

The TRCA-301E trial met its primary and all secondary endpoints. The primary endpoint of the TRCA-301E trial was an assessment of the long-term safety profile of veverimer versus placebo. In the veverimer group (versus placebo), we observed similar rates of treatment-emergent adverse events (81.3% versus 80.2%), fewer serious adverse events (1.8% versus 4.9%), and fewer adverse events leading to discontinuation (0 versus 1.2%). In addition, in the veverimer group (versus placebo) there were fewer subjects who discontinued study treatment (2.6% versus 9.8%) and a comparable rate of GI adverse events (21.4% versus 25.9%). No serious adverse events were assessed to be related to study drug by the trial investigator, Medical Monitor or Drug Safety and Pharmacovigilance Team.

Although not part of the primary endpoint, the statistical analysis plan for the TRCA-301E trial also specified a safety analysis comparing the veverimer and placebo groups for the time to the composite endpoint of death (all-cause mortality), dialysis/kidney transplant (renal replacement therapy) or a ≥50% decline in estimated glomerular filtration rate, or eGFR, (taken together, DD50) over the combined (TRCA-301/TRCA-301E trial) 52-week treatment period. Of the 124 subjects randomized to the veverimer group, 5 (4.0%) subjects had a DD50 event. There were no deaths in the veverimer group and one veverimer-treated subject initiated dialysis during the 52-week treatment period. Of the 93 subjects randomized to the placebo group, 10 (10.8%) subjects had a DD50 event, including four subjects who died and one who initiated dialysis during the 52-week treatment period. We observed an annualized DD50 incidence rate, calculated as 100 times the number of events divided by the total person-years, of 4.2% in the veverimer group versus 12.0% in the placebo group ($p = 0.0224$), representing a 65% reduction in the annualized event rate in veverimer-treated subjects versus subjects in the placebo group. The TRCA-301/TRCA-301E clinical trials were not designed or powered to assess this endpoint and no statistical alpha was allocated to the comparison; the studies enrolled only 217 subjects and followed them over a one-year treatment period to support the long-term safety and efficacy profile of veverimer.

TRCA-301 / TRCA-301E Trial Results (52 Weeks)
Prespecified Time-to-Event Analyses

Kaplan-Meier Plot of Time to First Occurrence of Death, Renal Replacement Therapy or ≥50% Decline in eGFR



The secondary endpoints of the TRCA-301E trial assessed the durability of effect of veverimer, both on serum bicarbonate levels and on measures of physical function, over the 52-week treatment period for those subjects who participated in the TRCA-301E trial. All were met with high statistical significance.

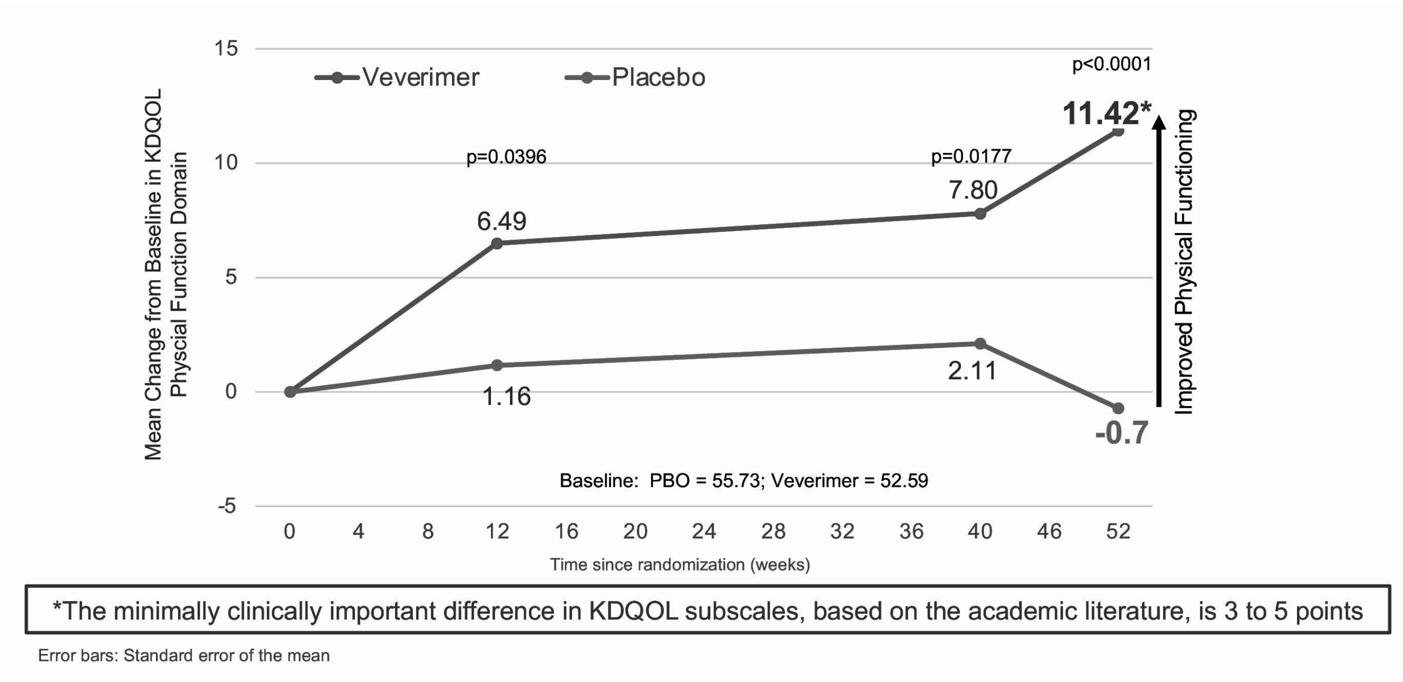
The durability of effect of veverimer was assessed in subjects who enrolled in the 40-week extension trial, TRCA-301E. In veverimer-treated subjects, the proportion of subjects achieving an increase of at least 4 mEq/L or normalization of serum bicarbonate was similar at Week 12 and Week 52 (61% and 63%, respectively). Similarly, the magnitude of the change in serum bicarbonate from baseline to Week 12 and to Week 52 were similar in veverimer-treated subjects (4.6 mEq/L and 4.7 mEq/L, respectively). However, rather than remaining stable, the corresponding values for the placebo group increased from Week 12 to Week 52 (22% and 38%; 1.7 mEq/L and 2.7 mEq/L, respectively). The reason that the treatment effect remained stable in veverimer-treated subjects but increased in placebo-treated subjects from Week 12 to Week 52 is not known; however, the discontinuation rate was ~3-fold higher in the placebo group and this may have contributed. It is also possible that being in the trial may have resulted in more attention paid to diet and lifestyle factors in the placebo group. Notwithstanding the results observed in the placebo group, we saw no waning of the effect of veverimer on serum bicarbonate over the 1-year treatment period in TRCA-301E.

Measures of physical function were assessed through the self-reported responses to the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test. Improvement from baseline to end of treatment in the self-reported responses to the KDQOL Physical Functioning Survey was significantly greater in the veverimer group (11.4 points) compared to the placebo group (-0.7 points), with a between-group difference of 12.1 points in favor of veverimer ($p<0.0001$). The 11.4-point improvement in the veverimer group exceeded the 3- to 5-point change cited in the literature as the minimal clinically important difference for KDQOL subscales.

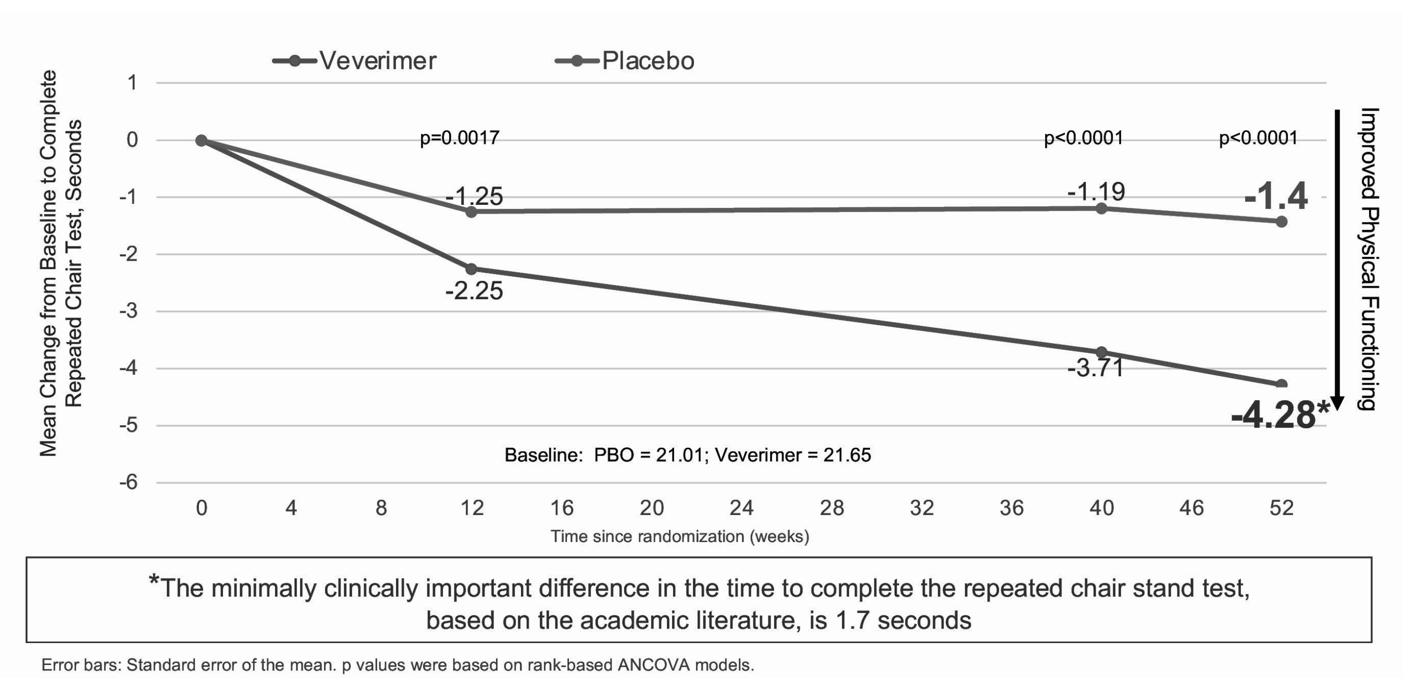
Improvement from baseline to end of treatment in physical function using the Repeated Chair Stand Test was also significantly greater in the veverimer group (4.3 seconds faster) compared to the placebo group (1.4 seconds faster), with a between-group difference of 2.9 seconds in favor of veverimer ($p<0.0001$). The placebo-adjusted improvements in favor of veverimer-treated subjects in the two measures of physical function at Week 52 approximately doubled compared to the results at week 12 observed in the parent trial, TRCA-301. The 4.3-second improvement in the time to complete the Repeated Chair Stand Test exceeded the 1.7-second improvement cited in the literature as the minimal clinically important difference for improvement in this measure of objective physical function. We believe the results from the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test are consistent with each other and both indicate a clinically meaningful improvement in physical function and related aspects of quality of life for veverimer-treated subjects.

TRCA-301 / TRCA-301E Trial Results (52 Weeks)
Clinically Meaningful Improvement in Physical Function

KDQOL Physical Function Domain



Repeated Chair Stand Test

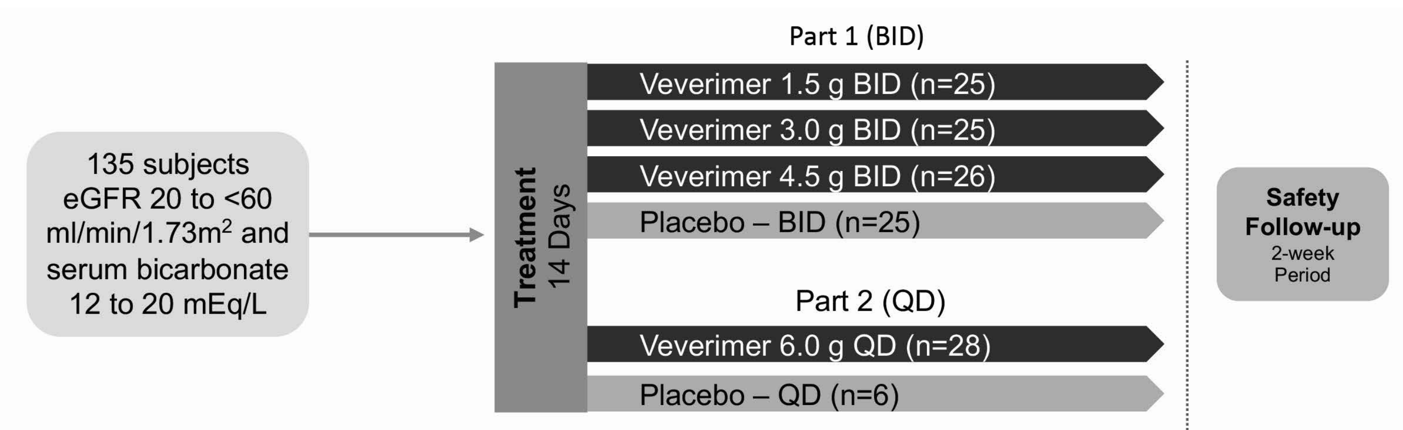


Academic literature describes CKD as a clinical model of premature aging, indicating that patients with CKD often experience many of the complications of aging, but at younger ages than the general population. This includes elevated rates of aging-related disorders, including markedly reduced physical function compared to adult populations of the same age. This is a major problem because impaired physical function leads to significant morbidity, including high rates of falls and fractures, and is also a risk factor for death. Therefore, preserving physical function is critical in patients with CKD. Dr. Matthew Abramowitz, Associate Professor of Medicine at the Albert Einstein College of Medicine, has conducted a post-hoc analysis of age-related physical function improvements that were observed with veverimer in our TRCA-301E long-term extension trial. First, the analysis showed that at baseline, 45% of our trial population was slower in performing the Repeated Chair Stand Test than the average 80 to 89-year old, despite an average age of 62 years. Second, the mean improvement of 4.3 seconds in Repeated Chair Stand Test time observed in veverimer-treated subjects in the TRCA-301E trial was greater than the difference in mean expected test-time performance between individuals in their 80s and those in their 60s, suggesting that the 4.3 second improvement in test time observed in veverimer-treated subjects is equivalent to an approximately 20-year reduction in aging-related physical functioning. Dr. Abramowitz concluded that interventions that improve physical function in patients with CKD have the potential to restore a substantial proportion of age-predicted loss of performance.

TRCA-101 Phase 1/2 Clinical Trial

In 2016, we completed our Phase 1/2 trial, TRCA-101, a 135-subject, double-blind, randomized, placebo-controlled trial of veverimer. In this trial, subjects received either placebo or one of four different dosing regimens of veverimer for two weeks as shown in the diagram below:

Veverimer Phase 1/2 Clinical Trial

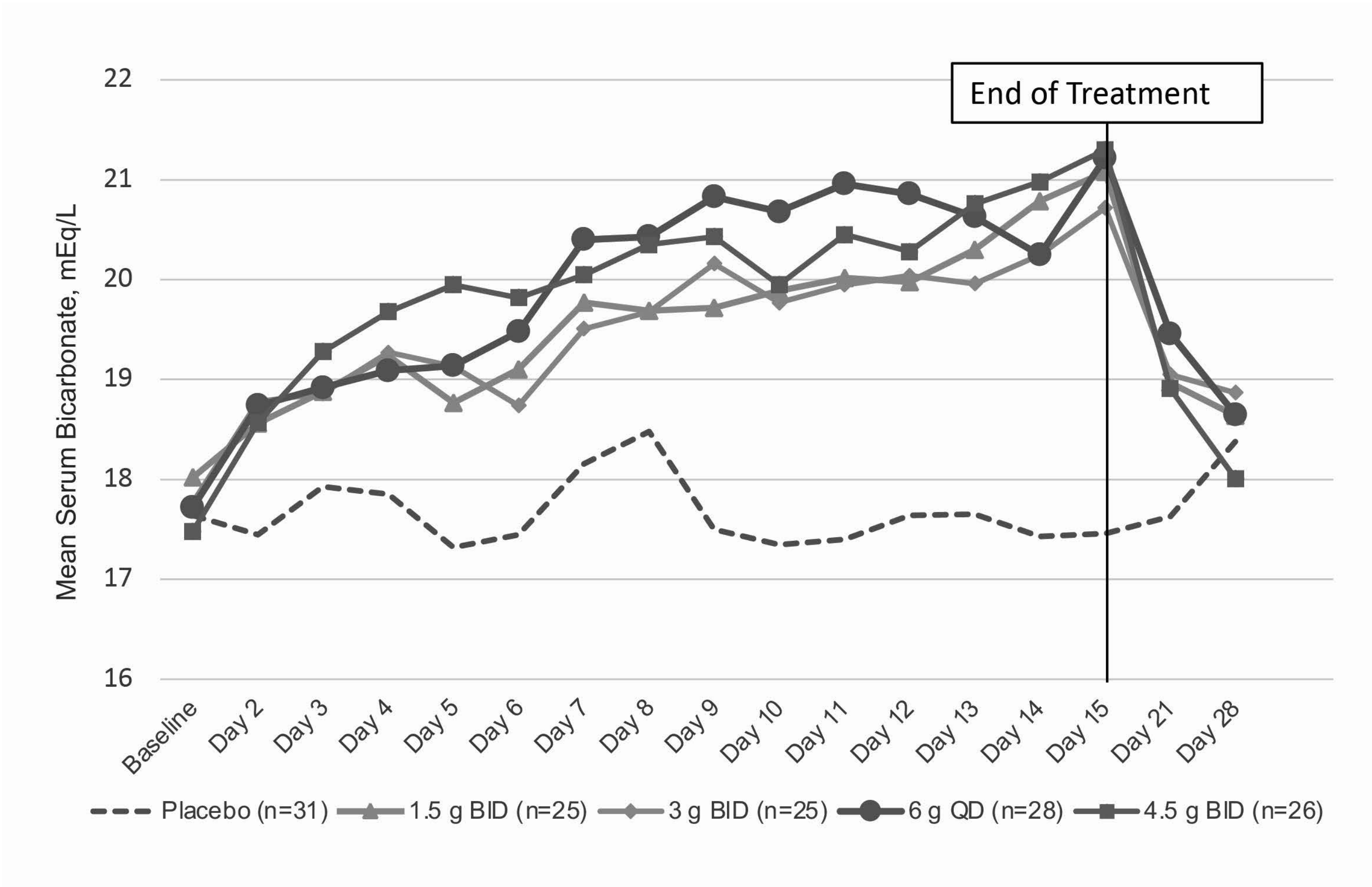


BID = Twice daily, QD = Once daily

The subjects were patients with Stage 3 or 4 CKD with serum bicarbonate levels at baseline between 12 and 20 mEq/L. The treatment groups were demographically well matched, and the mean serum bicarbonate levels at baseline ranged between 17.5 and 18.0 mEq/L across the treatment groups. Comorbid conditions of the subjects enrolled in TRCA-101 included 93% of patients with hypertension, 70% with type 2 diabetes, 29% with left ventricular hypertrophy and 21% with congestive heart failure. We conducted the trial at five in-patient clinical research units where the subjects were monitored for the duration of the 2-week treatment period. During the 16-day in-unit residence (including the 14-day treatment period), clinical trial subjects were given a diet controlled for protein, caloric content, anions, cations and fiber, in accordance with dietary recommendations for patients with CKD. The potential renal acid load, or PRAL, value was calculated for the daily meal plans to ensure that the trial diet was neither acidic nor basic. Daily PRAL values averaged 0.8 mEq/day. Average protein intake during the trial was 0.7 g/kg/day.

The primary objective of this trial was to assess the safety and tolerability of veverimer across a selection of doses in subjects with CKD and metabolic acidosis. The secondary objective was to evaluate efficacy. The serum bicarbonate levels of subjects were measured on a daily basis. Statistically significant increases in serum bicarbonate levels were observed in all veverimer-treated groups within 24 to 72 hours of initiation of therapy. After 14 days of treatment, the mean increase in serum bicarbonate levels from baseline in each of the veverimer-treated groups was between 2.95 and 3.83 mEq/L, with a mean serum bicarbonate increase of 3.3 mEq/L in the combined veverimer group. All these results were statistically significant (p-value < 0.0001), as were the increases from baseline as compared to the placebo group, whose mean serum bicarbonate level decreased by 0.18 mEq/L. The serum bicarbonate levels of all subjects were measured during the off-treatment follow-up period. In the veverimer-treated groups, the mean levels had reverted to near baseline levels after two weeks off treatment.

Veverimer Significantly Increased Mean Serum Bicarbonate Throughout the 2-week Treatment Period, with Serum Bicarbonate Rapidly Returning Toward Baseline After Treatment Discontinuation



In our Phase 1/2 trial, veverimer was well-tolerated. All subjects completed treatment and remained in the trial through the applicable follow-up period. All treatment emergent adverse events, or TEAEs, were mild or moderate, and there were no serious adverse events. The most common TEAE was diarrhea which was reported by 20.2% of veverimer-treated subjects as compared to 12.9% of subjects in the placebo group. All cases of diarrhea were mild, self-limited, and none required treatment. There were no apparent effects of veverimer on parameters, such as sodium, calcium, potassium, phosphate, magnesium, or low-density lipoprotein observed in the trial that would indicate off-target effects of veverimer. There were no apparent effects on vital signs, such as blood pressure, heart rate, respiratory rate or temperature, or body weight. The results of this trial were published in the Clinical Journal of the American Society of Nephrology (Bushinsky, et al., 2018).

Nonclinical Studies

We have conducted a range of nonclinical in vivo and in vitro studies to assess the mechanism of action, pharmacology, pharmacokinetics, and toxicology of veverimer.

Nonclinical in vitro and in vivo pharmacology studies demonstrated robust proton and chloride binding and retention by the veverimer polymer resulting in removal of hydrochloric acid from the body. In vitro studies demonstrated that veverimer can selectively bind and retain chloride under conditions that mimic the pH, transit times, and ionic content of various compartments of the GI tract. The marked binding capacity and selectivity for chloride observed with veverimer in vitro translates into in vivo pharmacological effects. Removal of acid by veverimer results in a dose-dependent increase in mean serum bicarbonate, as observed in rats with adenine-induced nephropathy and low serum bicarbonate. A significant increase in fecal chloride relative to controls suggests that veverimer retained its functional integrity during transit through the rat GI tract. This study in an animal model of CKD illustrated the potential of veverimer to correct depleted serum bicarbonate levels, the hallmark of metabolic acidosis.

Safety pharmacology assessments of the central nervous, respiratory, cardiovascular, and GI systems did not identify any veverimer-related adverse effects at oral doses up to 4 g/kg (central nervous system, respiratory) and up to 2 g/kg (GI) in rats and at 2 g/kg (cardiovascular) in dogs.

Lack of veverimer absorption from the GI tract was demonstrated in both rats and dogs administered a single oral dose of radiolabeled [^{14}C]-veverimer. Because radioactivity was not observed in the plasma of either species, metabolism was not evaluated. The lack of absorption, in conjunction with the in vivo pharmacology study in rats, supports that veverimer is not metabolized or degraded but maintains functional, and therefore, structural integrity during transit through the GI tract following oral administration. The results of the radiolabeled veverimer absorption, distribution, metabolism, and excretion, or ADME, studies demonstrating a lack of oral bioavailability is consistent with the physicochemical properties of veverimer (insolubility in aqueous and organic solvents, particle size averaging 100 micrometers in diameter, and particle stability).

Repeat-dose, GLP toxicology studies of up to 26 weeks duration in rats and 39 weeks duration in dogs demonstrated that veverimer has a very low order of toxicity and was well tolerated. There were no effects on male or female reproductive organs and local GI tolerance was good. The no observed adverse effect level, or NOAEL, in both the rat and dog in the chronic toxicity studies was the highest dose of 2 g/kg/day; this dose of veverimer is 13-fold higher than the highest proposed human dose of 9 g/day (0.15 g/kg/day based on a 60-kg patient). We also established that the polymer has no effect on the absorption of fat-soluble vitamins, such as A, D2, D3, and E. Reproductive toxicity studies indicate there are no adverse veverimer-related effects on maternal reproductive function. Upon a resubmission of our NDA for veverimer, we are prepared to discuss the embryofetal development and teratogenicity data with the FDA with respect to pregnancy label language. We do not expect these discussions to lead to any change in the pregnancy risk statement in the anticipated label due to the non-absorbed nature of veverimer. Veverimer was not mutagenic or clastogenic when evaluated in genotoxicity studies. Given the non-absorbed nature of veverimer, we were granted a waiver from FDA for fertility and early embryonic development (Segment I) and peri/postnatal development (Segment III) reproductive toxicity and carcinogenicity studies.

Drug-drug Interaction Studies

Veverimer is not systemically absorbed; therefore, its potential for DDIs is limited to those that occur in the GI tract (i.e., direct binding or indirect effects resulting from transient increases in gastric pH). We assessed the potential for DDIs with veverimer both in vitro and in vivo in healthy subjects.

In vitro binding to veverimer was evaluated with 16 drugs of varying molecular weight and charge. Human DDI studies were conducted with the 2 drugs (furosemide, aspirin) that showed the most in vitro binding to veverimer. The effect of veverimer on gastric pH was measured continuously in vivo in healthy subjects using a microelectrode pH probe placed in the gastric compartment. Human DDI studies were conducted with 3 orally administered drugs with pH-dependent solubility (dabigatran, furosemide, warfarin).

Veverimer did not bind to any of the positively charged, neutral or zwitterionic drugs tested in vitro. It bound to three small (Molecular Weight <332 Da), negatively charged drugs (aspirin, ethacrynic acid, furosemide); these interactions were reduced or eliminated in the presence of physiologically relevant concentrations of chloride. We tested aspirin and furosemide in vivo in human DDI studies conducted in healthy volunteers and these drugs showed a change in exposure of < 20% when co-administered with veverimer.

Veverimer increased gastric pH by approximately 3 and 1.5 pH units in fasted and fed subjects, respectively. The increase in gastric pH was short-lived, with a peak within 1 hour after dosing and a return to baseline after approximately 1.5 hours and approximately 3 hours under fasting and fed conditions, respectively. The effect of veverimer on gastric pH was similar in the presence and absence of omeprazole. The bioavailability of orally administered drugs that are weak acids and weak bases can be affected by changes in gastric pH. Therefore, the clinical relevance of the transient increase in gastric pH caused by veverimer was evaluated in vivo in human DDI studies conducted in healthy volunteers using three drugs with pH-dependent solubility: furosemide (weak acid), dabigatran (weak base) and warfarin (weak acid). These drugs showed a change in exposure of < 20% when co-administered with veverimer.

Based on the results of our DDI studies, we do not believe we need to recommend dosing separation for co-administered drugs with veverimer, either due to direct binding interactions or due to pH sensitivity. We believe it is reasonable to propose dosing instructions for veverimer that do not include any dose separation recommendations for other oral medications. However, if veverimer is approved for use by the FDA, the ultimate instructions in the prescribing information regarding co-administration of veverimer with other oral medications will be subject to FDA review and approval.

Veverimer Regulatory Pathway

Our regulatory goal is to obtain FDA approval through the Accelerated Approval Program based upon veverimer's effect on serum bicarbonate or traditional approval based upon veverimer's effect on slowing CKD progression and/or on improving physical functioning in patients with metabolic acidosis associated with CKD.

The FDA's Accelerated Approval Program allows for drugs for serious conditions that address an unmet medical need to be approved based on a surrogate endpoint that is reasonably likely to predict clinical benefit. Surrogate endpoints are used instead of clinical outcomes in some clinical trials. Surrogate endpoints are used when the clinical outcomes might take a very long time to study, or in cases where the clinical benefit of improving the surrogate endpoint, such as controlling blood pressure, is well understood. Clinical trials are needed to show that surrogate endpoints can be relied upon to predict, or correlate with, clinical benefit. Surrogate endpoints that have undergone this testing are called validated surrogate endpoints and those are accepted by the FDA as evidence of benefit.

Surrogate endpoints that the FDA determines are reasonably likely to predict clinical benefit but are not yet validated may be used to support approval, in some cases. This is accomplished through the FDA's Accelerated Approval Program, which is intended to provide patients with serious diseases more rapid access to promising therapies. Because such surrogate endpoints have not been validated, sponsors relying on them to support an accelerated approval are generally required to verify the predicted clinical benefit of their products with confirmatory postmarketing clinical trials.

We believe that veverimer meets the requirements for the FDA's Accelerated Approval Program based upon meeting the following three criteria:

- Treatment of a Serious Condition: There is evidence that the progression of CKD to ESRD is a serious condition and the chronic treatment of metabolic acidosis may slow the progression of CKD.

- Meaningful Advantage over Available Therapy: There is an unmet need for chronic therapies that slow progression to ESRD in patients with CKD and metabolic acidosis. There are no FDA-approved chronic treatments for metabolic acidosis and there exists a large population of patients with metabolic acidosis and CKD.

- Demonstrates an Effect on an Endpoint That Is Reasonably Likely to Predict Clinical Benefit: There are a number of prospective and retrospective studies that show that serum bicarbonate is an appropriate surrogate endpoint and that increasing serum bicarbonate is reasonably likely to predict slowing of progression of CKD.

As an alternative to approval through the Accelerated Approval Program, we may pursue approval of veverimer through the traditional approval pathway based upon veverimer's effect on the slowing of CKD progression or improving physical functioning. To satisfy the requirements for traditional approval we would be required to provide the FDA with sufficient data about clinical efficacy and safety in a sufficient number of subjects to permit the FDA to evaluate the overall benefit-risk relationship of veverimer and to provide adequate information for the labeling of veverimer. In most cases, the FDA requires at least two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the product candidate. A single Phase 3 clinical trial may be sufficient in certain circumstances, including (1) where the clinical trial is a large multicenter clinical trial demonstrating internal consistency and a statistically persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second clinical trial would be practically or ethically impossible or (2) when in conjunction with other confirmatory evidence.

We submitted our New Drug Application, or NDA, for veverimer through the Accelerated Approval Program in August 2019, and in August 2020, we received a Complete Response Letter, or CRL, from the FDA related to our NDA for veverimer. According to the CRL, the FDA is seeking additional data beyond the TRCA-301/TRCA-301E trial regarding the magnitude and durability of the treatment effect of veverimer on the surrogate marker of serum bicarbonate and expressed concern regarding whether the demonstrated effect size would be reasonably likely to predict clinical benefit. In addition, the CRL questioned the applicability of the treatment effect to the U.S. population and the practice of medicine in the United States. The FDA also expressed concern as to the reliability of the findings given that the findings for the TRCA-301/TRCA-301E trial were driven by a single, high-enrolling trial site located in Eastern Europe. The CRL did not raise any concerns related to FDA's completed inspection of the highest enrolling clinical trial site in the TRCA-301/TRCA-301E trial and there was no FDA Form 483 issued. There were no safety, clinical pharmacology/biopharmaceutics, CMC, or non-clinical issues identified in the CRL. The CRL provided multiple options for resolving the identified deficiencies, including submission of the data from at least one additional adequate and well-controlled trial demonstrating the efficacy of veverimer for the treatment of metabolic acidosis associated with CKD.

We held an End-of-Review Type A meeting, or Type A meeting, with the FDA's Division of Cardiology and Nephrology, or the Division, in October 2020. The Division agreed, in principle, that an interim analysis of serum bicarbonate data from the VALOR-CKD trial proposed by Tricida could address the Division's concerns regarding the reliability of the TRCA-301/TRCA-301E trial data and the relevance of those trial findings to the U.S. population provided certain conditions were met. Based on other feedback from the FDA during the Type A meeting, we believed the Division would also require evidence of veverimer's effect on CKD progression from a near-term interim analysis of the VALOR-CKD trial for accelerated approval and that the FDA would be unlikely to rely solely on serum bicarbonate data for determination of efficacy. Accordingly, we submitted a Formal Dispute Resolution Request, or FDRR, solely requesting that the Office of New Drugs, or OND, find that the magnitude of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis associated with CKD and that it can therefore serve as the basis for accelerated approval.

In February 2021, the OND issued a decision on our FDRR. While the OND acknowledged that the TRCA-301 and TRCA-301E trials met their serum bicarbonate endpoints with statistical significance, the OND denied the appeal. In its Appeal Denied Letter, or ADL, the OND not only addressed the issue of magnitude of serum bicarbonate change, but cited all of the deficiencies in the CRL in concluding that the data provided in support of the veverimer NDA did not support approval through the Accelerated Approval Program. The OND concluded that the magnitude of the increases in serum bicarbonate levels shown in the TRCA-301/TRCA-301E trial were not of sufficient size or duration to establish that treatment with veverimer would be reasonably likely to provide a discernible reduction in CKD progression. In addition, the OND found that the intended confirmatory trial, VALOR-CKD (also known as TRCA-303), was underpowered to detect a 13% reduction in slowing of CKD progression. This finding was based on information included in the initial NDA submission, including the placebo-subtracted LS mean change from baseline in serum bicarbonate observed in the TRCA-301/TRCA-301E trial and the original Predictive MA Model. The OND also raised concerns regarding the robustness of the study results given that the veverimer NDA was supported by a single registrational trial (TRCA-301/TRCA-301E), which must, alone, provide persuasive evidence of benefit. Specifically, the OND noted concerns around adequate blinding, the trial results being strongly influenced by a single site, and the majority of sites for the TRCA-301/TRCA-301E trial being in Eastern Europe, where differences in patient management, including concomitant medications and diet, might affect the treatment response to veverimer and raise a concern of the applicability to a U.S. patient population. The OND also stated that, while trial results in the TRCA-301/TRCA-301E trial showed improvement in two patient-reported measures, the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test, the OND viewed this subjective data from a single trial with skepticism in the absence of data from a second trial with similar results and noted that both endpoints would require rigorous blinding to support robust conclusions. However, the OND noted that both of these changes, if eventually established by one or more additional trials, would indicate a potentially meaningful benefit of veverimer treatment—especially in CKD patients who have physical functional impairments. Separate from the ADL, we previously received feedback from the Division of Clinical Outcome Assessment, or DCOA, that reliance on these physical function endpoints for approval may require further validation.

Based on the ADL, we believe that we now have greater clarity on the potential approval of veverimer through the Accelerated Approval Program. The OND suggested that we meet with the Division to discuss submission of Week 52 serum bicarbonate results from the full randomized trial population of VALOR-CKD and that the trial should include a substantial portion of patients from the United States or from regions with “US-like” patients. If the results of this trial were to demonstrate that veverimer provides a meaningfully larger treatment effect than seen in the TRCA-301/TRCA-301E trial, then this trial, along with the results from the TRCA-301/TRCA-301E trial, could address the concerns raised in the CRL regarding the limitations and the size of the treatment response observed in the TRCA-301/TRCA-301E trial. However, whether the extent of increase in serum bicarbonate in any subsequent submission based on VALOR-CKD would support accelerated approval will remain a review issue, and will, in part, reflect the Division’s assessment of the adequacy (i.e., power) of VALOR-CKD to detect the anticipated treatment effect of CKD progression in a reasonable timeframe.

Although the ADL provides greater clarity on the potential path for approval of veverimer through the Accelerated Approval Program, we believe the timeline to meet the requirements for accelerated approval as suggested in the ADL may not result in the most rapid development path for veverimer. For example, if either of the planned interim analyses in VALOR-CKD for early stopping for efficacy results in positive renal outcomes data, this data could be available before the week 52 serum bicarbonate data from the fully enrolled VALOR-CKD trial suggested in the ADL and could potentially serve as the basis for resubmission of the NDA. We are evaluating several options with respect to the VALOR-CKD trial that are focused on obtaining, prior to the end of 2022, additional data on the effect of veverimer on (1) CKD progression; (2) physical functioning; and (3) serum bicarbonate. We may explore the possibility of stopping the trial early for administrative reasons, which would allow analysis of the data using all alpha remaining at that time. In any event, we believe data from VALOR-CKD will be very important in furthering our understanding of the regulatory path for approval of veverimer. As such, we intend to continue the execution of the VALOR-CKD trial with consideration of both the accelerated and traditional approval pathways. Resubmission of the veverimer NDA may require additional clinical data beyond that provided by the VALOR-CKD trial. The FDA's acceptance of the VALOR-CKD data in support of an NDA resubmission, including its assessment of the magnitude and durability of the veverimer treatment effect across the various geographical regions where the study is conducted and the acceptability of the data from non-US countries or regions which will comprise a substantial proportion of the data from the trial, will ultimately be a review issue.

Market Opportunity

We estimate that there are approximately 3 million patients in the United States afflicted with metabolic acidosis and Stage 3 to 5 non-dialysis CKD and that approximately 1.1 million of such patients are under the care of a physician. Our initial target market will be focused on the approximately 600,000 patients with metabolic acidosis and CKD that are under the care of a nephrologist. We have identified approximately 5,000 nephrologists who treat approximately 80% of these patients. Given the demographics of the CKD patient population, these nephrologists are geographically concentrated on the west coast, the northeast and the southeast of the United States.

We have conducted multiple surveys of practicing nephrologists designed to understand their knowledge of the link between treating metabolic acidosis and the slowing of CKD progression. In a survey of 100 nephrologists, conducted in 2019, we found that over 80% believed that treating metabolic acidosis was moderately, very or extremely important to slow kidney disease progression.

We have also conducted multiple surveys of practicing nephrologists to quantify the expected market for veverimer, if approved. In a survey of 100 nephrologists, conducted in 2019, 79% indicated that they would definitely or probably prescribe veverimer, based on a veverimer target product profile which included information from the results of our TRCA-301E clinical trial that were published in The Lancet in June 2019.

We have also evaluated, through health and economic outcomes analyses, the potential savings to third-party payers and health benefits that could be derived through the treatment of patients with metabolic acidosis and CKD. In 2019, we completed a retrospective health economic study of pre-dialysis patients with Stage 3 to 5 CKD. The study evaluated renal outcome events and healthcare costs for 51,558 pre-dialysis patients with Stage 3 to 5 CKD derived from electronic health records, or EHRs, and corresponding medical claims from a national de-identified electronic medical record dataset over a 10-year period (2007 to 2017). The results of the study showed the following health impacts of metabolic acidosis over a 2-year period:

- 3 times higher likelihood of death: 31% of patients with metabolic acidosis and CKD at baseline died versus 10% of patients with CKD with normal serum bicarbonate at baseline;

- 3.6 times higher likelihood of starting dialysis: 18% of patients with metabolic acidosis and CKD at baseline started dialysis versus 5% of patients with CKD with normal serum bicarbonate at baseline; and

- 1.5 times higher likelihood to progress by 1 or more CKD stages: 38% of patients with metabolic acidosis and CKD at baseline progressed 1 or more stages of CKD versus 25% of patients with CKD with normal serum bicarbonate at baseline.

In addition, the results of the study showed that healthcare costs were approximately $40 thousand per patient per year higher for patients with metabolic acidosis versus patients that had normal serum bicarbonate levels. The results of the study also suggest that each 1 mEq/L increase in serum bicarbonate can be associated with a 7% decrease in monthly all-cause healthcare costs ($p<0.0001$). The potential savings to payers and health benefits derived through these analyses were independent of the patient's status with regard to CKD stage, albumin-to-creatine ratio, sex, age, race, diabetes, heart failure, hypertension or Charlson Comorbidity Score (an index of comorbidity burden).

Due to the absence of an FDA-approved product for chronic metabolic acidosis, we cannot model a treated versus untreated population for these health economic studies. As such, we relied on evaluating similar patient populations, contrasting those with metabolic acidosis and those with a normal serum bicarbonate level.

Additionally, we have conducted multiple surveys of third-party payers representing healthcare coverage for over 200 million U.S. lives. Based on our surveys, as the first and only potential FDA-approved therapy for the treatment of chronic metabolic acidosis and slowing of kidney disease progression in patients with metabolic acidosis associated with CKD, we believe the majority of third-party payers will provide coverage for veverimer, which may be subject to prior authorization and/or other forms of utilization management. We also plan to offer veverimer through both retail and specialty-pharmacy providers to help ensure appropriate physician support and patient access to therapy. In addition, we have evaluated the healthcare insurance coverage mix of our target patient population and we estimate that the majority of these patients will have healthcare insurance coverage through 1) Medicaid programs, Medicare with low-income subsidy programs or Veterans Administration/Department of Defense programs which typically cover prescriptions with a low co-pay obligation for patients or 2) a commercial healthcare insurance plan where we typically can provide co-pay assistance to patients.

Given the high unmet need for an FDA-approved chronic treatment for patients with metabolic acidosis and CKD, the broad understanding among nephrologists that treatment of metabolic acidosis can slow CKD progression, the favorable response from nephrologists to veverimer's target product profile, the potential health and economic benefits from treating metabolic acidosis, and our survey results which suggest that health insurers are open to providing coverage for veverimer, we believe that there is a significant opportunity for veverimer in the United States, if approved, as the first and only FDA-approved therapy for the treatment of chronic metabolic acidosis and slowing of kidney disease progression in patients with metabolic acidosis associated with CKD.

In addition, we believe there is a significant market opportunity for veverimer outside the United States, if approved. We intend to seek one or more partners with international sales expertise who can obtain regulatory approval and sell veverimer in target markets. We anticipate that, in certain markets, additional clinical trials of veverimer may be required to obtain regulatory approval and/or ensure market access.

Commercial Strategy and Plan

We plan to initially focus our commercial launch of veverimer, if approved, on a subset of 5,000 nephrologists in the United States who care for approximately 80% of the 600,000 patients with metabolic acidosis and CKD seen by nephrologists. We believe we can reach this target market using a nephrologist-focused sales force of approximately 80 to 90 individuals. Alternatively, we may seek to commercialize veverimer in the United States with one or more partners.

In 2020, we expanded our disease awareness campaign with extensive disease awareness outreach to engage with nephrologists. Our comprehensive disease awareness and education campaign is designed to communicate the existing evidence that increasing serum bicarbonate in patients with metabolic acidosis and CKD slows the progression of CKD and can potentially improve how patients feel and function. We believe the broad understanding of this evidence will help to establish and increase the urgency to treat patients with this serious condition. Our targeted digital placements in 2020 drove nephrologists to our disease education website, MetabolicAcidosisInsights.com. We sponsored disease-related publications and continuing medical education, or CME, courses, and added features to our Neph+ app that provide easy access to publicly available kidney disease treatment guidelines commonly used calculations for kidney disease and other informational resources for nephrologists.

If veverimer is approved, we plan to engage with nephrologists through multiple communication channels to provide them with the veverimer prescribing information and appropriate supplemental marketing materials to augment that information. This will include branded materials for distribution to nephrologists, a branded website, a nephrologist-focused digital marketing campaign, participation in congresses and nephrology-focused events, and speaker programs that educate nephrologists on current disease knowledge and treatment options.

We have also engaged with third-party payers to seek favorable coverage for veverimer, if approved. We have presented to third-party payers information about the design and results of our health economic study and shared veverimer clinical trial data in three separate third-party payer forums: 1) through an in-person survey involving 15 third-party payers covering over 200 million patient lives, 2) through a Payer Working Group Meeting involving four third-party payers representing over 150 million lives and 3) through face-to-face individual meetings with 126 third-party payers representing approximately 310 million lives. Third-party payers have indicated their perception of the likelihood of veverimer coverage is influenced by the following potential attributes of veverimer: first and only FDA-approved treatment, disease modifying, safe and efficacious and significant direct healthcare cost savings.

A number of peer-reviewed publications will provide support for our disease awareness campaign and the launch of veverimer, if approved. In 2019, the results of our TRCA-301 and TRCA-301E trials were published in The Lancet (March 2019 and June 2019). A compilation of the clinical evidence that treatment of metabolic acidosis slows CKD progression was published in Current Opinion in Nephrology and Hypertension (Goraya and Wesson, 2019) and a meta-analysis of the effects of treatment of metabolic acidosis in CKD was published in the Clinical Journal of the American Society of Nephrology, or CJASN (Navaneethan et al., 2019). A critical assessment of the data related to clinical effects of sodium from sodium chloride versus sodium bicarbonate in patients with CKD-induced metabolic acidosis was published in the American Journal of Kidney Diseases, or AJKD (Bushinsky, 2019). Six presentations reporting veverimer mechanism of action and clinical data as well as health economics and clinical outcomes research related to metabolic acidosis were reported at the 2019 ASN Kidney Week Meeting. In 2020, The Journal of Pharmacology and Experimental Therapeutics published data on the veverimer mechanism of action and a review of the mechanisms underlying metabolic acidosis-induced kidney damage in CKD was published in the Journal of American Society of Nephrology, or JASN, by Wesson et al. In addition, seven presentations were reported at the NKF Spring Clinical Meeting 2020 and 12 presentations were reported at the 2020 ASN Kidney Week Meeting describing the veverimer mechanism of action and clinical data as well as health economics and clinical outcomes research related to metabolic acidosis.

Manufacturing

Veverimer drug substance is a room-temperature stable, free flowing powder, composed of low-swelling, polymeric beads, approximately 100 micrometers in diameter. As a non-absorbed polymeric drug, veverimer is designed to be insoluble in water and organic solvents, and is characterized by its desired function, including high hydrochloric acid binding capacity and selectivity, and physical properties, such as minimal swelling. Characterization of the isolated intermediate and careful control of each process step define the structure of the polymer. Because the process to manufacture veverimer fundamentally defines the key polymer attributes for safety and efficacy, the process has been carefully monitored and optimized during scale-up.

Veverimer is manufactured using a two-step process. This two-step approach enables, in step one, the preparation of a crosslinked polymer having a high binding capacity, and in step two, further crosslinking for low swelling and selectivity for hydrochloric acid binding.

The resulting veverimer drug substance is converted into drug product by filling it into packets without the addition of excipients. Veverimer drug product is stored at room temperature. Stability studies demonstrated that veverimer is stable at room temperature for at least 12 months, and we are conducting registration stability studies that we anticipate will enable us to indicate on our label, if approved, that veverimer is stable at room temperature for up to 24 months.

We contract with third-party service providers to manufacture veverimer drug substance and veverimer drug product and to perform analytical testing services. We currently have no manufacturing facilities and limited personnel with manufacturing experience. We developed the process to manufacture veverimer drug substance in-house and have successfully transferred it to three manufacturers. We believe that there are a limited number of experienced contract manufacturers in the world capable of manufacturing a polymeric drug substance such as veverimer. We currently rely on Patheon Austria GmbH & Co KG, or Patheon, a subsidiary of Thermo Fisher Scientific, Inc., as our sole supplier for drug substance manufacturing and we have used two suppliers for drug product manufacturing. We entered into a multi-year Manufacturing and Commercial Supply Agreement with Patheon in October 2019. Patheon has agreed to manufacture and supply us with veverimer to support our initial commercialization efforts and clinical needs. We intend to initially commercialize with a single supplier for drug substance and a single supplier for drug product. Our business plan assumes that we will establish a regionally diverse and volume-appropriate portfolio of third-party manufacturers to reduce our dependency on single suppliers for drug substance and drug product in the future. We plan to continue to rely upon contract manufacturers and suppliers of raw materials for the commercial manufacture of veverimer if it is approved by regulatory authorities.

We have validated the veverimer drug substance manufacturing process at Patheon to produce veverimer in a batch size of approximately 700 kg. In addition, we have manufactured sufficient amounts of drug substance to support our ongoing VALOR-CKD trial. The process to manufacture drug product has also been validated.

Polymeric-based drugs like veverimer generally require large quantities of drug substance, as compared to small molecule drugs. Accordingly, we will require larger scale and/or multiple manufacturers of drug substance and drug product in order to manufacture sufficient quantities of veverimer to meet our anticipated market demand. We believe that our current production process can be optimized to meet our anticipated commercial needs without introducing changes to key veverimer properties, including binding capacity, selectivity for hydrochloric acid and non-absorption. We use acid binding, competitive anion binding and particle size measurement assays to confirm these properties. The scale of the first step in our drug substance manufacturing process, step one, is approximately 640 kg, and the scale of the second step in our drug substance manufacturing process, step two, is approximately 700 kg. We are continuing to work with our current manufacturer to further optimize and scale our drug substance manufacturing process with the intention of achieving additional manufacturing capacity as well as working to secure a second manufacturer of drug substance.

Our third-party service providers, their facilities and the veverimer used in our clinical trials or for commercial sale are required to be in compliance with current Good Manufacturing Practices, or cGMP. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and packaging containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The facilities manufacturing and testing our products must meet cGMP requirements and satisfy FDA or other authorities before any product is approved and before we can manufacture commercial products. Our third-party manufacturers are also subject to periodic inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of veverimer to assess compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties. These actions could have a material impact on the availability of veverimer. Contract manufacturers at times encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, manufacturing and process discoveries, and other know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications 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, continuing technological innovation, trademark protection and potential in-licensing opportunities to develop and maintain our proprietary position.

Veverimer was discovered by us utilizing our proprietary technology. We have filed several non-provisional and provisional patent applications, all owned by us, relating to veverimer in the United States, certain foreign countries, and the World Intellectual Property Organization that are directed to compositions-of-matter, dosage unit forms, methods-of-treatment, medical use, and methods of manufacture.

Our patent portfolio, which is solely owned by us, includes 126 patents issued in 2020 in 47 different countries, two issued U.S. composition of matter patents (U.S. Patent No. 9,205,107 B2 and No. 9,925,214 B2), four issued U.S. method of treatment patents (U.S. Patent Nos. 9,993,500 B2, 10,391,118 B2, 10,363,268 B2, and 10,369,169 B1), an issued Australian medical use patent (AU 2014274817 B2), an issued Australian composition of matter patent (AU 2019219800 B1), two issued European medical use patents (EP3 003 327 B1 and EP 3 578 185 B1), two issued European composition of matter patents (EP 3 287 133 B1 and EP 3 593 808 B1), an issued European method of manufacture patent (EP 3 229 816 B1), an issued Chinese composition of matter patent (ZL 2014 8 0032395.1), an issued Mexican medical use patent (MX 364785 B), issued Hong Kong medical use and composition patents (HK 1223288 A1 and HK 1251151, respectively), an issued Israeli medical use patent (IL 242758), an issued Russian use (Swiss-type) and composition patent (RU 2728778), an issued Russian method of manufacture patent (RU 2713416) and issued Japanese medical use and composition of matter patents (JP 6,453,860 B2 and JP 6759316 B2, respectively). Each of these issued patents is expected to expire in 2034 (with the exception of EP 3 229 816 B1, EP 3 593 808 B1 and RU 2713416, which are expected to expire in 2035), excluding any additional term resulting from patent term extension if the appropriate maintenance fees are paid.

In addition, we solely own other patent applications relating to veverimer (for example, composition of matter, dosage unit form, method-of-treatment, medical use and method of manufacture patent applications, where applicable) that are currently pending in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Mexico, Republic of Korea, Russia, and the United States. Certain of these patent applications are also pending in Malaysia, New Zealand, Singapore, South Africa and Taiwan. These currently pending patent applications, if they mature into issued patents in one or more of such jurisdictions, are expected to expire between 2034 and 2038, if the appropriate maintenance, renewal, annuity, and other government fees are paid.

Additional patent term for the presently-issued or later-issued patents may be awarded on a jurisdiction-by-jurisdiction basis. For example, additional patent term for U.S. patents may be awarded as a result of the patent term extension provision of the Hatch-Waxman Amendments of 1984, or the Hatch-Waxman Act. In the European Union member countries, a supplementary protection certificate, if obtained, provides a maximum five years of market exclusivity. In Japan, the term of a patent may be extended by a maximum of five years in certain circumstances.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are effective for 20 years from the earliest effective filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the USPTO delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. The actual protection afforded by a patent varies on a product by product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

We also protect our proprietary technology and processes, in part, by confidentiality and invention assignment agreements with our employees, consultants, scientific advisors and other contractors. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, alter our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have a material adverse impact on us.

Research and Development

We are conducting development activities to support our NDA for veverimer and manufacturing of commercial supply of veverimer. We invested $148.4 million, $133.0 million and $85.6 million in research and development for the years ended December 31, 2020, 2019 and 2018, respectively.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. We may face competition from large pharmaceutical and biotechnology companies, smaller pharmaceutical and biotechnology companies, specialty pharmaceutical companies, academic institutions, government agencies and research institutions and others.

Many of our competitors may have significantly greater financial, technical and human resources than we have. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if competitors develop or market products or other novel technologies that are more effective, safer or less costly than veverimer, or they may obtain regulatory approval for their products more rapidly than we may obtain approval for ours.

There are no therapies approved by the FDA for the chronic treatment of metabolic acidosis. We are aware that AstraZeneca is conducting a clinical trial to explore the use of sodium zirconium cyclosilicate in patients with hyperkalemia and metabolic acidosis associated with chronic kidney disease. The FDA has approved generic intravenous sodium bicarbonate solutions for the treatment of acute metabolic acidosis which may occur in severe renal disease, uncontrolled diabetes, and certain other disorders accompanied by a significant loss of bicarbonate; however, those therapies are used for short-term, hospital-based treatments and are not used in clinical practice to treat chronic metabolic acidosis. For many nephrologists, first-line management of metabolic acidosis in patients with CKD is to recommend a protein-restrictive diet. Retrospective analyses show that 3% to 15.0% of patients with metabolic acidosis and CKD use oral alkali supplementation, such as sodium bicarbonate, sodium citrate or, less frequently, potassium citrate. These supplements have not been approved by the FDA for the treatment of metabolic acidosis.

Government Regulation

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, postmarketing monitoring and reporting, and import and export of drug products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA Approval Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FFDCA, and implementing regulations. These laws and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, postmarketing monitoring and reporting, sampling, and import and export of drug products. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as clinical hold, FDA refusal to approve pending regulatory applications, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

The process required by the FDA before a drug may be marketed in the United States generally includes the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices, or GLP, and other applicable regulations;

- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin in the United States;

- performance of adequate and well-controlled human clinical trials according to Good Clinical Practice, or GCP, to establish the safety and efficacy of the product candidate for its intended use;

- submission to the FDA of an NDA for a new product;

- satisfactory completion of an FDA inspection, if conducted, of the facility or facilities where the product candidate is manufactured to assess compliance with the FDA's current Good Manufacturing Practices, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the drug product candidate's identity, strength, quality, purity, and potency;

- potential FDA inspection of the nonclinical and clinical trial sites;

- potential FDA inspection of us and vendors involved in the generation of the data in support of the NDA; and

- FDA review and approval of the NDA.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product candidate or disease. A clinical hold may occur at any time during the life of an IND and may affect one or more specific trials or all trials conducted under the IND.

Nonclinical tests include laboratory evaluation of the product candidate's chemistry, formulation, and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product candidate. The conduct of the nonclinical tests must comply with federal regulations and requirements, including GLP. The results of nonclinical testing are submitted to the FDA as part of an IND along with other information, including information about product candidate's chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term nonclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational product to healthy volunteers or subjects under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with GCP, an international standard meant to protect the rights and health of subjects and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. subjects and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial subjects. The trial protocol and informed consent information for subjects in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. The study sponsor may also suspend a clinical trial at any time on various grounds, including a determination that the subjects are being exposed to an unacceptable health risk.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the product candidate is usually into healthy human subjects, and the product candidate is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the product candidate for a particular indication, dosage tolerance, and optimal dosage, and to identify common adverse effects and safety risks. If a product candidate demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of subjects, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the product candidate and to provide adequate information for the labeling of the product candidate. In most cases, the FDA requires at least two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the product candidate. A single Phase 3 clinical trial may be sufficient in certain circumstances, including (1) where the clinical trial is a large multicenter clinical trial demonstrating internal consistency and a statistically persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second clinical trial would be practically or ethically impossible or (2) when in conjunction with other confirmatory evidence.

A drug product candidate being studied in clinical trials may be made available for treatment of individual patients, in certain circumstances. Pursuant to the 21st Century Cures Act, or Cures Act, which was signed into law in December 2016, the manufacturer of an investigational product for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational product.

During the development of a new product candidate, sponsors are given opportunities to consult with the FDA at certain points; specifically, prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These interactions can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide feedback on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trials that they believe will support the approval of the new product candidate.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and the manufacturer must develop methods for testing the quality, purity and potency of the product candidate. 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 proposed shelf life. After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all nonclinical, clinical, and other testing and a compilation of data relating to the product candidate's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, and the applicant under an approved NDA is also subject to annual prescription drug program fees. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may refuse to file any NDA that it deems incomplete or not properly reviewable at the time of submission and may identify necessary additional information. In this event, the NDA must be resubmitted with the additional information and the resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is filed, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review product candidates are reviewed within ten months of the date the FDA files the NDA if the product is a new molecular entity, or NME, or within ten months of submission for a non-NME; most applications for priority review product candidates are reviewed within six months of the date the FDA files the NDA if the product is an NME and within six months of submission if it is a non-NME. Priority review can be applied to a product candidate that the FDA determines has the potential to treat a serious or life-threatening condition and, if approved, would be a significant improvement in safety or effectiveness compared to available therapies. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission. This late-submitted information is typically requested by FDA.

Among other things, the FDA reviews an NDA to determine whether the product is safe and effective for its intended use and whether the product candidate is being manufactured in accordance with cGMP. The FDA may also refer applications for novel product candidates, or product candidates that present difficult questions of safety or efficacy, to an advisory committee, typically a panel that includes clinicians and other experts for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA may inspect the facility or the facilities at which the product candidate is manufactured. The FDA will not approve the product candidate 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. To assure GCP and cGMP compliance, an applicant must incur significant expenditures of time, money and effort in the areas of training, record keeping, production, and quality control.

After the FDA evaluates the NDA and manufacturing facilities, it issues either an approval letter or complete response letter, or CRL. A CRL generally describes the specific deficiencies in the application identified by the FDA and may require substantial additional testing, or information, in order for FDA to reconsider the application. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. If a CRL is issued, the applicant may either resubmit the NDA, addressing the deficiencies identified in the letter, or withdraw the application. Prior to taking either of those actions, an applicant may decide to submit a Formal Dispute Resolution Request, or FDRR.

The FDRR process offers sponsors, which includes NDA applicants, a mechanism for resolving scientific and/or medical disputes that cannot be resolved at the division level. A CRL is a regulatory action that the FDA considers appropriate for formal dispute resolution. An FDRR must include information adequate to explain the nature of the scientific and/or medical dispute and to allow the deciding official to determine the necessary steps needed to resolve the matter quickly and efficiently. Because internal Agency review of a decision that has been appealed by a sponsor must be based on the same information as was relied on to make the original decision, no new information should be submitted as part of an FDRR. As part of the FDRR process, the sponsor can request a meeting with the deciding official. If a meeting is granted, the deciding official should provide a decision on the FDRR to the sponsor within 30 calendar days after the meeting is held. If the deciding official provides an interim response or requests additional information, the timeframe for a decision on the FDRR may be delayed. If the sponsor's FDRR is denied at one management level, the sponsor can escalate its appeal to the next higher management level in the FDA's chain of command.

If, or when, the deficiencies identified in a CRL have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing of the drug in the United States with specific prescribing information for specific indications.

Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific indications and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA also may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk evaluation and mitigation strategy, or REMS, or otherwise limit the scope of any approval. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the product. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. In addition, the FDA may require confirmatory postmarketing trials, sometimes referred to as "Phase 4" clinical trials, designed to further assess a product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Foreign Clinical Studies to Support an IND or NDA

The FDA may accept as support for an IND or NDA a well-designed, well-conducted, non-IND foreign clinical trial if it was conducted in accordance with GCP and the FDA is able to validate the data from the trial through an on-site inspection, if necessary. A sponsor or applicant who wishes to rely on a non-IND foreign clinical trial must submit supporting information to the FDA to demonstrate that the trial conformed to GCP.

Regulatory applications based solely on foreign clinical data meeting these criteria may be approved if the foreign data are applicable to the U.S. population and U.S. medical practice, the trials have been performed by clinical investigators of recognized competence, and the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or other appropriate means. Failure of an application to meet any of these criteria may result in the application not being approvable based on the foreign data alone.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Expedited Development and Review Programs

The FDA has various programs, including Fast Track Designation, Priority Review Designation, Accelerated Approval Program and Breakthrough Therapy Designation, which are intended to expedite or simplify the process for reviewing product candidates. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will be lengthened. Generally, product candidates that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track Designation is a process designed to facilitate the development and expedite the review of product candidates to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority Review Designation is designed to give a product candidate that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness, an initial review within six months as compared to a standard review time of within ten months of the date the FDA receives (in the case of a non-NME) or files (in the case of an NME) the NDA.

Although Fast Track Designation and Priority Review Designation do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track Designation product candidate and expedite review of the application for a Priority Review Designation product candidate.

In addition to the Fast Track Designation and Priority Review Designation Programs discussed above, a sponsor may request Breakthrough Therapy Designation of a product candidate if the product candidate is intended, alone or in combination with one or more other therapeutics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A request for Breakthrough Therapy Designation should be submitted concurrently with, or as an amendment to, an IND, but ideally no later than the End-of-Phase 2 meeting.

Accelerated Approval Program

Under the accelerated approval regulations, the FDA may grant accelerated approval to a product for a serious or life-threatening disease or condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. Products approved through the Accelerated Approval Program must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

The Accelerated Approval Program is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, while the effect on the surrogate endpoint occurs more rapidly. The FDA will not grant approval through the Accelerated Approval Program to products that meet standards for traditional approval.

The evidence to support the determination that an endpoint is reasonably likely to predict clinical benefit may include epidemiological, pathophysiological, therapeutic, pharmacologic, or other evidence developed using biomarkers, for example, or other scientific methods or tools. The FDA considers all relevant evidence and may consult external experts, as needed. Important factors for the agency's consideration include the disease process and the relationship between the drug's effect and the disease process.

Approval through the Accelerated Approval Program is subject, however, to the requirement that the applicant conduct additional confirmatory postmarketing clinical trials to verify and describe the drug's clinical benefit, where there is uncertainty as to the relationship of the surrogate endpoint to the clinical benefit, or of the observed clinical endpoint to ultimate outcome. Typically, clinical benefit is verified when confirmatory clinical trials show that the drug provides a clinically meaningful positive therapeutic effect, that is, an effect on how a patient feels, functions, or survives. The FDA may require that any confirmatory trial be initiated or substantially underway prior to the submission of an application through the Accelerated Approval Program. And, if the sponsor does not pursue the confirmatory trial with due diligence or such confirmatory trial fails to confirm the drug's clinical profile or risks and benefits, the FDA may withdraw its approval of the drug. The FDA may also withdraw the approval if other evidence demonstrates that the product is not safe or effective. All promotional materials for product candidates approved through the Accelerated Approval Program are subject to prior review by the FDA. The FDA has issued labeling instructions specific to the program. For example, if a drug is approved based on a surrogate endpoint through the program, its labeling should include a succinct description of the limitations of usefulness of the drug and any uncertainty about anticipated clinical benefits. False or misleading promotional materials may also lead to expedited withdrawal of approval.

Orange Book Listing, Patent Term Restoration and Marketing Exclusivity

Orange Book Listing

Under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch Waxman Amendments, NDA applicants are required to identify to FDA each patent whose claims cover the applicant's drug or approved method of using the drug. Upon approval of a drug, the applicant must update its listing of patents to the FDA in timely fashion and each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book.

Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredient(s), strength, route of administration, and dosage form as the reference listed drug and has been shown to be bioequivalent to the reference listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved under the ANDA pathway are commonly referred to as "generic equivalents" to the reference listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug pursuant to each state's laws on drug substitution.

The ANDA applicant is required to certify to the FDA concerning any patents identified for the reference listed drug in the Orange Book. Specifically, the applicant must certify to each patent in one of the following ways: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid, unenforceable or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid or unenforceable, is called a Paragraph IV certification. For patents listed that claim an approved method of use, under certain circumstances the ANDA applicant may also elect to submit a statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent, which is called a Section VIII statement. If the applicant does not challenge the listed patents through a Paragraph IV certification, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA-holder and patentee(s) once the ANDA has been accepted for filing by the FDA (referred to as the "notice letter"). The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice letter. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months from the date the notice letter is received, expiration of the patent, the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed, or a decision in the patent case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired. In some instances, an ANDA applicant may receive approval prior to expiration of certain non-patent exclusivity if the applicant seeks, and FDA permits, the omission of such exclusivity-protected information from the ANDA prescribing information.

Patent Term Restoration

After approval, owners of relevant drug patents may apply for up to a five-year patent extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch- Waxman Act. The allowable patent term extension is calculated as half of the product's testing phase-the time between IND and NDA submission-and all of the review phase-the time between NDA submission and approval, up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years and only one patent may have a patent term extension.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the U.S. Patent and Trademark Office must determine that approval of the product candidate covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a product candidate for which an NDA has not been submitted.

Market Exclusivity

Market exclusivity provisions under the FFDCA also can delay the submission or the approval of certain applications. The FFDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A product candidate is a new chemical entity if the FDA has not previously approved any other new product candidate containing the same active moiety, which is the molecule or ion responsible for the action of the product candidate substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such product candidate where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FFDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing product candidate. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for product candidates containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Postmarketing Requirements

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 FDA review and approval. In addition, the FDA may under some circumstances require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA under some circumstances has the power to prevent or limit further marketing of a product based on the results of these postmarketing programs.

Once an NDA is approved, a product will be subject to certain post-approval requirements and continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences associated with the product;
- providing the FDA with updated safety and efficacy information;
- therapeutic sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- registration and listing requirements; and
- complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

Manufacturers, their subcontractors, and other entities involved in the manufacture of approved products, are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP, including data integrity requirements, and other laws. The FDA periodically inspects manufacturing facilities to assess compliance with ongoing regulatory requirements, including cGMP, which impose extensive procedural, substantive and record-keeping requirements on NDA sponsors and third-party manufacturers and certain of their subcontractors. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require FDA approval before being implemented. FDA regulations would also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and our third-party manufacturers. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. Regulatory authorities may withdraw product approvals, request product recalls or take other judicial or administrative actions such as warning letters, suspension of manufacturing, seizures of products, injunctive actions or other civil penalties, if a company fails to comply with the statutory and regulatory requirements, if it encounters problems after initial marketing or if previously unrecognized problems are subsequently discovered.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

In addition, drug manufacturers in the United States must comply with applicable provisions of the Drug Supply Chain Security Act and provide and receive product tracing information, maintain appropriate licenses, ensure they only work with other properly licensed entities, and have procedures in place to identify and properly handle suspect and illegitimate product.

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and veverimer. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations will be changed or what the effect of such changes, if any, may be.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services (such as the Office of Inspector General and the Health Resources and Service Administration), the U.S. Department of Justice, or the DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs may have to comply with the federal Anti-Kickback Statute, the federal False Claims Act, or FCA, the privacy and security provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, recommending or arranging for the purchase, lease or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between therapeutic product manufacturers on one hand and prescribers, purchasers, formulary managers, and anyone in a position to purchase or recommend the product on the other. There are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing, ordering or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or the PPACA , to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the PPACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA (discussed below).

The federal false claims and civil monetary penalty laws, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal healthcare programs, including Medicare and Medicaid, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes “any request or demand” for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses.

HIPAA created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payers, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute, the PPACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Also, many states have similar, and typically more prohibitive, fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Additional information about the scope of these requirements and potential penalties is provided under *“Risk Factors - We may be subject to healthcare laws, regulation and enforcement; our failure to comply with these laws or regulations, or our potential involvement in enforcement activities, could have a material adverse effect on our results of operations and financial conditions”* of this Annual Report on Form 10-K. Additionally, to the extent that veverimer may in the future be sold in a foreign country, we may be subject to similar foreign laws.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes 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, independent contractors, or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways, are often not pre-empted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

We expect that veverimer, if approved, may be eligible for coverage under Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain pharmaceutical products, that are medically necessary to treat a beneficiary's health condition. In addition, veverimer may be covered and reimbursed under other government programs, such as Medicaid and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program. As part of the requirements to participate in these government programs, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average manufacturer price, or AMP, and best price. There are penalties for failing to provide timely and accurate price reporting to the government, and the Right Rebate Act (effective April 2019) imposes additional penalties for knowingly misclassifying a covered outpatient drug under the Medicaid Drug Rebate Program.

Additionally, the federal Physician Payments Sunshine Act, or the Sunshine Act, within the PPACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to "Covered Recipients", or to entities or individuals at the request of, or designated on behalf of, Covered Recipients and to report annually certain ownership and investment interests held by physicians and their immediate family members. The term Covered Recipients currently includes U.S.-licensed-physicians and teaching hospitals, and, for reports covering payments and other transfers of value during calendar year 2021 and submitted on or after January 1, 2022, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. In addition, many states also govern the 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.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other 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.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of veverimer, if approved. In the United States and in foreign markets, sales of veverimer, if and when we receive regulatory approval for commercial sale, will depend, in part, on the extent to which third-party payers provide coverage and establish adequate reimbursement levels for such products. In the United States, third-party payers include federal and state healthcare programs, private managed care providers, commercial health insurers and other organizations. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payers are critical to new product acceptance.

Our ability to commercialize veverimer successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which therapeutics they will pay for and establish reimbursement levels. Coverage and reimbursement by a third-party payer may depend upon a number of factors, including the third-party payer's determination that use of a therapeutic 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.

We cannot be sure that reimbursement will be available for veverimer and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the indications for which the product is approved by the FDA or comparable foreign regulatory authorities. Reimbursement may impact the demand for, or the price of, veverimer, if approved.

Third-party payers are increasingly challenging the price, examining the medical necessity, and reviewing the cost effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for veverimer may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost effectiveness of veverimer, in addition to the costs required to obtain FDA approvals. Veverimer may not be considered medically necessary or cost-effective. Obtaining coverage and reimbursement approval of a product from a government or other third-party payer is a time-consuming and costly process that could require us to provide to each payer supporting scientific, clinical and cost-effectiveness data for the use of veverimer on a payer-by-payer basis, with no assurance that coverage and adequate reimbursement will be obtained. A payer's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payer's determination to provide coverage for a product does not assure that other payers will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. In addition, prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payers and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to veverimer in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize veverimer.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. 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. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross- border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of veverimer, if approved, for commercial sale may suffer if the government and third-party payers fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes in the United States has increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to effectively sell product candidates for which marketing approval is obtained. Policy makers and payers in the United States and elsewhere, have undertaken efforts to contain healthcare costs, improve quality, and expand patient access to healthcare items and services. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, the PPACA substantially changed and continues to impact healthcare financing and delivery by both government payers and private insurers. Among the PPACA provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs that began in 2011;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price, or AMP, for most branded and generic drugs, respectively, and a cap on the total rebate amount for single source and innovator drugs at 100.0% of the product's AMP;
- the Medicare Part D coverage gap discount program, where as a condition for the manufacturers’ outpatient drugs to be covered under Medicare Part D program, manufacturers must agree to offer 70.0% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period;
- extension of manufacturers’ Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care plans;
- expansion of the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding mandatory eligibility categories for individuals with income at or below 138.0% of the federal poverty level, thereby potentially increasing manufacturers’ Medicaid rebate liability;
- expansion of the entities eligible for discounts under the 340B Drug Discount Program;
- establishment of the Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- expansion of healthcare fraud and abuse laws, including the FCA and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a separate 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;

- requirements to report certain financial arrangements with physicians and teaching hospitals, and beginning with reports submitted on January 1, 2022, financial arrangements with physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse midwives;

- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians;

- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending; and

- a licensure framework for follow on biologic products.

While the Biden Administration has recently signaled its intent to pursue policies strengthening the PPACA, there have been legal and judicial, Congressional, and political challenges to certain aspects of the PPACA, as well as efforts by the Trump administration to repeal and replace certain aspects of the PPACA. President Trump signed at least two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the PPACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Although two courts have ruled that this repeal renders the individual mandate unconstitutional, the Supreme Court granted certiorari in March 2020, and in November 2020 heard oral arguments in an appeal to address this issue and the effect of the individual mandate repeal on the constitutionality of the PPACA as a whole. A decision is expected later in 2021. Additionally, on December 20, 2019, President Trump signed appropriations legislation for fiscal year 2020 that repealed the so called "Cadillac" tax on certain high-cost employer-sponsored insurance plans, for tax years beginning after December 31, 2019; the annual fee imposed on certain third-party providers based on market share, for calendar years beginning after December 31, 2020; and the medical device excise tax on nonexempt medical devices, for sales after December 31, 2019. In the future, there may be additional challenges and amendments to the PPACA. It remains to be seen precisely what new legislation will provide, when it will be enacted, and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare, including the cost of pharmaceutical products.

We anticipate that the PPACA, if substantially maintained in its current form, will continue to result in additional downward pressure on coverage and the price that we receive for veverimer, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize veverimer. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Further legislation or regulation could be passed that could harm our business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the PPACA was enacted. For example, the Budget Control Act of 2011, as amended, requires automatic reductions in Medicare payments for all items and services, including prescription drugs, of up to 2.0% per fiscal year. This sequestration took effect beginning on April 1, 2013 and will remain in effect through 2030 unless additional Congressional action is taken, with the exception of a temporary suspension by Congress for the period from May 1, 2020 through March 31, 2021 in response to the coronavirus pandemic. Moreover, the Bipartisan Budget Act of 2018 among other things, amended the PPACA, effective January 1, 2019, to increase from 50.0% to 70.0% the point-of-sale discount to eligible beneficiaries during their coverage gap period that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Additionally, there has been increasing legislative, administrative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal legislation and regulations designed to, among other things, lower drug pricing, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer-sponsored patient support programs, and reform government program reimbursement methodologies for drugs. For example, included in the Consolidated Appropriations Act, 2021 were several drug price reporting and transparency measures, such as a new requirement for certain Medicare plans to develop tools to display Medicare Part D prescription drug benefit information in real time and for group and health insurance issuers to report information on pharmacy benefit and drug costs to the Secretaries of HHS, Labor and the Treasury. Additionally, in December 2020, CMS issued a final regulation amending the Medicaid Drug Rebate Program. The rule implements changes to align existing regulations with statutory amendments enacted pursuant to the PPACA, and includes provisions affecting price reporting related to manufacturer-sponsored patient assistance programs subject to PBM accumulator programs, certain value-based purchasing arrangements, line extensions, and authorized generics. Because certain parts of this rule were scheduled to take effect after January 20, 2021, those provisions are subject to the "Regulatory Freeze Pending Review" memorandum issued by the Biden Administration on January 20, 2021, which freezes implementation of certain regulations and guidance documents issued by the Trump administration that had not yet taken effect as of January 20, 2021 and, for rules that have been issued, recommends opening a new comment period for interested parties.

At the state level, legislatures and agencies are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including constraints on pricing, discounting and reimbursement; restrictions on certain product access and marketing; cost disclosure and transparency measures that require detailed reporting of drug pricing and marketing information both at product launch and in the event of a price increase; and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. For example, the state of California passed legislation that requires drug manufacturers to notify the state at least 60 days prior to instituting price increases and Maryland passed legislation to create a drug pricing review commission that will evaluate drug cost and recommend setting an upper limit or cap for therapies deemed too expensive. We cannot predict what other reforms may ultimately be implemented at the federal or state level or the effect of any future legislation or regulation and, accordingly, face uncertainties that may result from additional reforms and their impact on our operations. Further, the implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize veverimer, if approved.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, and to devise and maintain an adequate system of internal accounting controls for international operations.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

European Union/Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials, manufacturing and any future commercial sales, promotion and distribution of veverimer. Whether or not we obtain FDA approval to market veverimer, we must obtain the requisite approvals from regulatory authorities in foreign jurisdictions prior to the commencement of clinical trials or marketing of the products in those countries.

Even if a product obtains FDA marketing approval, most foreign jurisdiction require that the investigational product undergo national requirements related to clinical trials and authorization processes, similar to those in the United States. With respect to clinical trials, certain countries outside of the United States have a similar process that requires the submission of a clinical trial application, much like the IND, prior to the commencement of human clinical trials. In the European Union, or the EU, for example, before starting a clinical trial, a valid request for authorization must be submitted by the sponsor to the competent authority of the EU Member State(s) in which the sponsor plans to conduct the clinical trial, as well as to independent Ethics Committee(s). A clinical trial may generally commence only once the relevant Ethics Committee(s) has (have) issued a favorable opinion and the competent authority of the EU Member State(s) concerned has (have) not informed the sponsor of any grounds for non-acceptance. Failure to comply with applicable EU requirements may subject a company to the rejection of the request and the prohibition to start a clinical trial. Clinical trials conducted in the EU (or the data to be used to support a marketing authorization application in the EU) must be conducted in accordance with applicable laws, GCP and GMP rules, International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, or ICH, guidelines and be consistent with ethical principles. Competent authorities of EU Member States regularly conduct GCP inspections to verify the sponsor's compliance with applicable rules. The sponsor is required to record all adverse events which are reported to it by investigators and submit, upon request, such records to the EU Member State in which the clinical trial is being conducted. The sponsor is also required to record and report to the relevant national competent authorities and to the Ethics Committee(s) information about suspected serious unexpected adverse reactions (i) as soon as it becomes aware of suspected serious unexpected reactions, and (ii) yearly of all suspected serious adverse reactions having occurred over the past year and to report on the subjects' safety.

The authorization of a clinical trial may be suspended or revoked by EU Member States in their respective territory if the conditions in the request for an authorization are no longer met, or if an EU Member State has information raising doubts about the safety or scientific validity of the clinical trial. Various penalties exist in EU Member States for non-compliance with the clinical trial rules and related requirements, for example with respect to data protection and privacy. If we or our potential collaborators fail to comply with applicable EU regulatory requirements, we may also be subject to damage compensation and civil and criminal liability.

The way clinical trials are authorized and conducted in the EU will undergo a major change when the new EU Clinical Trials Regulation (Regulation 536/2014) comes into application, according to the European Commission currently expected in December 2021. The new Clinical Trials Regulation is aimed at simplifying and streamlining the approval of clinical trials in the EU. The main characteristics of the Regulation include: a streamlined application procedure via a single entry point; a single set of documents to be prepared and submitted for the application; as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different EU Member States. The current regime under the EU Member States' national legislation implementing the Clinical Trials Directive (Directive 2001/20/EC) will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

Requirements to conduct a clinical trial in the United Kingdom are similar. Specifically, sponsors of clinical trials taking place in the UK must obtain authorization. The clinical trial must be registered in a public database (e.g., ISRCTN registry or ClinicalTrials.gov) and the sponsor must obtain a favorable opinion from a UK ethics committee. The United Kingdom recognizes ethics and regulatory approvals for clinical trials that were granted through the EU processes before December 31, 2020, but any trial commencing after January 1, 2021 must obtain UK authorization. Non-compliance with applicable requirements may equally result in the clinical trial authorization being suspended or revoked, and sponsor may be subject to civil and criminal liability.

As in the United States, no medicinal product may be placed on the EU and UK markets unless a marketing authorization has been issued. In the UK, the Medicines and Healthcare products Regulatory Agency, or MHRA, assesses the safety, quality and efficacy of medicinal products based on applications for marketing authorizations and grants an authorization if the risk-benefit balance is considered favorable. In the EU, medicinal products may be authorized in different ways, depending on certain criteria: the national authorization procedure (i.e., via the EU Member States' national authorization procedure, which later allows for application via the mutual-recognition procedure), the centralized authorization procedure (i.e., at EU level), or the decentralized authorization procedure (i.e., authorization of a product that is not yet authorized in the EU, which can simultaneously be authorized in several EU Member States). Products submitted for approval via the national procedure must follow the national authorization procedures, which vary from Member State to Member State. Products submitted for approval via the centralized procedure (compulsory for certain products and indications; e.g., human medicines containing a new active substance to treat HIV or AIDS, advanced-therapy medicines, and orphan medicines, and optional for certain other products and indications) are assessed by the Committee for Medicinal Products for Human Use, or CHMP, a committee within the European Medicines Agency, or EMA. The CHMP assesses, inter alia, whether a medicine meets the necessary quality, safety and efficacy requirements and whether it has a positive risk-benefit balance. Products submitted for approval via the decentralized procedure, as for the mutual-recognition procedure, must first undergo an assessment performed by one Member State, or reference Member State, which another Member State may approve.

Various penalties and sanctions exist in different EU Member States for non-compliance with the EU marketing authorization procedure. In addition, for centrally authorized products the European Commission may also impose financial penalties on the holders of marketing authorizations if they fail to comply with certain obligations in connection with the authorizations as well as pharmacovigilance rules (a fine up to 5% of the marketing authorization holder's turnover in the EU in the preceding business year for an infringement; daily penalty payments up to 2.5 % of the marketing authorization holder's average daily turnover in the EU in the preceding business year, pending cessation of an infringement; and a fine up to 0.5% of the marketing authorization holder's turnover in the EU in the preceding business year for e.g. failure to cooperate or supply of misleading information to authorities). If we or our potential collaborators fail to comply with applicable EU or other foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Similar rules apply in the UK.

As described above, coverage and reimbursement status of veverimer, if approved, are provided for by the national laws of EU Member States. The requirements may differ significantly across the EU Member States. Also, at EU Member State level, actions have been taken to enact transparency laws regarding payments between pharmaceutical companies and health care professionals, or HCPs.

We are subject to European data protection laws, including the EU General Data Protection Regulation 2016/679, or GDPR (as implemented by EU Member States and the UK). The GDPR which came into effect on May 25, 2018, establishes requirements applicable to the processing of personal data (i.e., data which identifies an individual or from which an individual is identifiable), affords various data protection rights to individuals (e.g., the right to erasure of personal data) and imposes potential penalties for serious breaches of up to 4.0% annual worldwide turnover or €20 million, whichever is greater. Individuals (e.g., study subjects) also have a right to compensation for financial or non-financial losses (e.g., distress). The GDPR increases our responsibility and liability in relation to personal data that we process, and additional mechanisms put in place to address compliance with the GDPR must be kept under review as the legislative and regulatory landscape for data protection in Europe continues to evolve.

For other countries outside of the European Union and the United Kingdom, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements. The requirements and process governing the conduct of clinical trials, product licensing, privacy and data protection, pricing and reimbursement also vary from country to country.

Human Capital Resources

As of December 31, 2020, we had 64 full-time employees. Our employees are not represented by labor unions or covered by collective bargaining agreements. We maintain good relationships and retain our employees through our competitive equity, cash compensation and benefits programs which are designed to attract, retain, and motivate our employees.

We compete in the highly competitive biotechnology and pharmaceuticals industries. Attracting, retaining and developing skilled and experienced employees in research and development, regulatory affairs, clinical operations, technical operations, and other positions is crucial to our ability to compete effectively. Our human capital resources objectives include, attracting, retaining, motivating, developing and integrating our highly skilled and qualified new and existing employees.

Corporate Information

We were incorporated under the laws of the state of Delaware on May 22, 2013 and were granted certification of qualification in the state of California on August 5, 2013. Our principal offices are located at 7000 Shoreline Court, Suite 201, South San Francisco, California. Our telephone number is (415) 429-7800. Our website address is tricida.com. The information in, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 12(a) or 15(d) of the Exchange Act are available, free of charge, on or through our website as soon as reasonably practicable after such reports and amendments are electronically filed with or furnished to the SEC. The SEC maintains an Internet site that contains, reports, proxy and information statements and other information regarding our filings at sec.gov. The contents of these websites are not incorporated into this filing. Further, references to the URLs for these websites are intended to be inactive textual references only.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with the other information contained elsewhere in this Annual Report on Form 10-K, including Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" and Part II, Item 8. "Financial Statements," as well as our other filings with the Securities and Exchange Commission, or SEC, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could materially and adversely affect our business, financial condition, results of operations, cash flows and prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Summary of Risk Factors

Investing in our securities involves a high degree of risk. You should carefully consider all of the risks discussed in Part I, Item 1A. "Risk Factors" of this Annual Report on Form 10-K, not just those discussed under this "Summary of Risk Factors" before making a decision to invest in our securities. The following is a list of some of these risks:

- We have a limited operating history, have incurred significant losses in each year since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have only one investigational drug candidate, veverimer (also known as TRC101), which is still in clinical trials and has no commercial sales.

- We are dependent on the success of veverimer and, if we are unable to successfully develop, obtain regulatory approval for and commercialize veverimer, or continue to experience significant delays in doing so, our business will be materially harmed. Based on the Complete Response Letter, or CRL, received from the FDA in August 2020, and the Appeal Denied Letter, or ADL, received in February 2021, we believe the criteria and pathway for resubmission and approval of our New Drug Application, or NDA, for veverimer is more clear, but the timing of any such approval is uncertain. The regulatory approval process is highly uncertain, and we may not obtain approval through the Accelerated Approval Program or the traditional approval process, as required for the commercialization of veverimer. We could be required to conduct additional nonclinical and clinical studies and trials beyond those that we currently contemplate, which would increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, marketing approval for veverimer.

- The design of our on-going renal outcomes trial, VALOR-CKD (also known as TRCA-303), may be impacted by additional information that becomes available to us or by clinical data generated while the VALOR-CKD trial is ongoing, including data that may affect key assumptions regarding sample size, endpoints, duration or the underlying standard of care, in which case we may be required to modify the design of this trial or conduct additional clinical trials.

- A continued delay in obtaining approval could further delay commercialization of veverimer and adversely impact our ability to generate revenue, our business and our results of operations. The denial of regulatory approval for veverimer could mean that we need to cease operations altogether. Even if we are able to obtain approval of veverimer through the Accelerated Approval Program, if our renal outcomes trial, VALOR-CKD, which would serve as a confirmatory postmarketing trial, does not verify clinical benefit, or if we are subject to and do not comply with rigorous postmarketing requirements, the FDA may seek to withdraw the approval.

- Together with our limited operating history and our requirements for substantial additional financing to achieve our goals, including the completion of our on-going clinical trial, VALOR-CKD, it is difficult to assess our future viability. We require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, our commercialization efforts of veverimer, or further reduce or cease our operations altogether. Our current debt obligations expose us to risks that could adversely affect our business, operating results, overall financial condition and may result in further dilution to our stockholders. For example, transactions relating to our Convertible Senior Notes may dilute the ownership interest of our stockholders, and the conditional conversion feature of the Convertible Senior Notes, if triggered, may adversely affect our financial condition and operating results.

- The incidence and prevalence of the target patient population for veverimer are based on estimates and third-party sources. If the market opportunity for veverimer is 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 might be materially and adversely affected.

- We do not have commercial capabilities that would be required for a successful commercial launch of veverimer, if approved. Development of such capabilities would require significant financial investment as well as recruitment of key personnel. An inability to develop such commercial capabilities or a delay, could meaningfully impact our business.

- Our business operations are heavily dependent on third parties to perform functions critical to our success. We currently rely completely on third-party suppliers to manufacture, package and label our clinical drug supply of veverimer drug substance and drug product, and we intend to rely completely on third parties to produce, package and label commercial supply of veverimer drug substance and drug product, if approved. Any interruption or performance failure on the part of our suppliers could delay the development and potential regulatory approval and commercialization of veverimer. In addition, we have relied and continue to rely on third parties, particularly CROs, to conduct and complete our clinical trials, including our on-going clinical trial, VALOR-CKD. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize veverimer, if approved.

- An epidemic or pandemic disease outbreak, including the COVID-19 outbreak, could disrupt our business operations as well as the business or operations of our third-party manufacturers and testing laboratories, our CROs, clinical data management organizations, medical institutions and clinical investigators, the FDA or other regulatory authorities, or other third parties with whom we conduct business, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

- If we fail to attract and keep senior management and other key personnel, we may be unable to successfully develop veverimer, conduct our clinical trials and commercialize veverimer, if approved.

- Our stock price may be volatile and fluctuate substantially and you may not be able to resell shares of our common stock at or above the price you paid.

Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

We have a limited operating history, have incurred significant losses in each year since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have only one investigational drug candidate, veverimer (also known as TRC101), which is still in clinical trials and has no commercial sales. We received a Complete Response Letter, or CRL, from the FDA related to our New Drug Application, or NDA, for veverimer. Further, the Office of New Drugs, or OND, issued an Appeal Denied Letter, or ADL, to our Formal Dispute Resolution Request, or FDRR. Together with our limited operating history, these factors make it difficult to assess our future viability.

We are a pharmaceutical company focused on the development and commercialization of our investigational drug candidate, veverimer (also known as TRC101), a non-absorbed, orally-administered polymer designed to treat metabolic acidosis in patients with chronic kidney disease, or CKD. We have only a limited operating history upon which you can evaluate our business and prospects. Our net losses were $264.8 million, $176.8 million and $102.8 million for the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $633.8 million. Pharmaceutical product development is a highly speculative undertaking, entails substantial upfront capital expenditures and involves a substantial degree of risk, including the risk that a potential drug candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. We have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical industry. To date, we have focused principally on developing our investigational drug candidate, veverimer. We have no products approved for commercial sale and have not generated any revenue from product sales or other arrangements to date and neither will we for the foreseeable future. We continue to incur significant research and development and other expenses related to our ongoing operations. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue our development of, and seek regulatory approval for, veverimer, prepare for potential commercialization of veverimer and continue to operate as a public company and comply with legal, accounting and other regulatory requirements.

If veverimer is not successfully developed or commercialized, including because we are unable to address the deficiencies identified in the CRL from the FDA related to our NDA or the issues raised in the ADL issued by the OND to our FDRR because of a lack of capital or otherwise, or if we do not generate enough revenue following marketing approval, we will not achieve profitability and our business may fail. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or commercialization efforts of veverimer, or to cease operations altogether.

We are currently advancing veverimer through clinical development. As of December 31, 2020, we had working capital of $279.8 million and cash, cash equivalents and investments of $332.3 million. We believe that we will continue to expend substantial resources for the foreseeable future as we continue clinical development, seek regulatory approval, and prepare for the commercialization of veverimer and develop any other drug candidates we may choose to pursue in the future. These expenditures will include costs associated with research and development, sales and marketing, conducting nonclinical and clinical studies and trials, obtaining regulatory approvals, and manufacturing and supply. In addition, other unanticipated costs may arise, including in connection with attempting to address the deficiencies identified in the CRL from the FDA related to our NDA or the issues raised in the ADL issued by the OND on our FDRR and resubmission of the NDA. Because the outcome of any clinical trial and the regulatory approval process is highly uncertain, we cannot reasonably estimate the actual expenditures necessary to successfully complete the development, regulatory approval process and commercialization of veverimer.

We believe that our existing cash, cash equivalents and investments of $332.3 million will allow us to fund our operating plan through at least the next 12 months. However, we have based these estimates on assumptions that may prove to be wrong, and we could spend our available capital resources much faster than we currently expect or require more capital to fund our operations than we currently expect. Moreover, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations. Such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

- the time and cost necessary to obtain regulatory approvals for veverimer and any future drug candidates that we develop, in-license or acquire;
- our ability to obtain approval for veverimer through the Accelerated Approval Program or traditional approval process;
- the costs associated with addressing the deficiencies identified in the CRL from the FDA related to our NDA or the issues raised in the ADL issued by the OND on our FDRR and resubmission of our NDA, and any increased costs associated with raising capital in light of such deficiencies or resulting delays;

- the progress, timing, scope and costs of conducting our nonclinical and clinical studies and trials, including our ongoing VALOR-CKD trial, in a timely manner, or potential future nonclinical and/or clinical studies and trials we may be required to conduct;
- the costs associated with conducting additional clinical trials for veverimer, if any, that the FDA and/or foreign regulatory agencies may require us to conduct prior to approval to market veverimer;
- the costs of postmarketing studies or clinical trials for veverimer that could be required by regulatory agencies or that we might otherwise choose to conduct;
- the costs of obtaining commercial supplies of veverimer;
- our ability to successfully commercialize veverimer;
- the manufacturing, selling and marketing costs associated with veverimer, including the cost and timing of establishing our sales and marketing and medical affairs capabilities;
- the cost of fulfilling our minimum contractual obligations to our suppliers and vendors;
- the timing and costs related to the optimization and scale-up of our manufacturing processes for veverimer and commercial supply of veverimer;
- the amount and timing of sales, royalties and other revenue from veverimer, if approved, including the sales price and the availability of adequate third-party reimbursement;
- the costs of operating as a public company;
- the costs associated with any product recall that could occur;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing products or treatments;
- the cash requirements of any future acquisitions or discovery of future drug candidates, if any;
- the costs of hiring and retaining personnel;
- the time and cost necessary to respond to technological and market developments;
- the potential impact of pandemics, including COVID-19, on the health care system, financial markets and economy generally and on our business in particular, including the potential impact on enrollment and retention of patients in or the power of our VALOR-CKD trial;
- the costs of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation; and
- the costs of defending against claims brought against the Company, its management and/or its Board of Directors, including litigation costs associated with shareholder, class action and derivative suits.

We cannot assure you that anticipated additional financing will be available to us on favorable terms, or at all. Our current Term Loan contains negative covenants that restrict our ability to obtain additional debt financing. Any future debt financing into which we enter may impose upon us covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. Although we have been successful in obtaining financing through the issuance of our equity securities and debt financing, we cannot assure you that we will be able to do so in the future. If we are unable to raise additional capital to fund our clinical development of veverimer, and commercialization, if approved, and other business activities, we could be forced to significantly delay, scale back or abandon one or more clinical development programs or commercialization efforts and curtail or cease our operations. In addition, our ability to achieve profitability or to respond to competitive pressures would be significantly limited.

Risks Related to Our Business

We are dependent on the success of veverimer, our only investigational drug candidate. If we are unable to successfully develop, obtain regulatory approval for and commercialize veverimer, or experience significant delays in doing so, our business will be materially harmed.

To date, we have invested all of our efforts and financial resources in the research and development and potential commercial launch of veverimer, which is our only investigational drug candidate. Our business and future success depends on our ability to successfully develop, obtain regulatory approval for, and commercialize veverimer. We are currently conducting a renal outcomes clinical trial, VALOR-CKD (also known as TRCA-303), to determine if veverimer slows CKD progression in patients with metabolic acidosis associated with CKD. Our VALOR-CKD trial is a randomized, double-blind, placebo-controlled, time-to-event trial. In May 2018, we completed our multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial for veverimer, known as TRCA-301. The TRCA-301 trial enrolled 217 subjects with metabolic acidosis and CKD. Eligible subjects who completed the 12-week treatment period in our Phase 3 trial were invited to continue in our 40-week extension trial, TRCA-301E, and we completed the TRCA-301E trial in March 2019. While these trials met their primary and secondary endpoints, the FDA has indicated that these trials alone are not sufficient to support approval of veverimer. Further, we cannot assure your that any foreign regulatory agency will approve veverimer for marketing.

We submitted our New Drug Application, or NDA, for veverimer through the Accelerated Approval Program in August 2019, and in August 2020, we received a Complete Response Letter, or CRL, from the FDA related to our NDA for veverimer. According to the CRL, the FDA is seeking additional data beyond the TRCA-301/TRCA-301E trial regarding the magnitude and durability of the treatment effect of veverimer on the surrogate marker of serum bicarbonate and expressed concern regarding whether the demonstrated effect size would be reasonably likely to predict clinical benefit. In addition, the CRL questioned the applicability of the treatment effect to the U.S. population and the practice of medicine in the United States. The FDA also expressed concern as to the reliability of the findings given that the findings for the TRCA-301/TRCA-301E trial were driven by a single, high-enrolling trial site located in Eastern Europe. The CRL did not raise any concerns related to FDA’s completed inspection of the highest enrolling clinical trial site in the TRCA-301/TRCA-301E trial and there was no FDA Form 483 issued. There were no safety, clinical pharmacology/biopharmaceutics, CMC, or non-clinical issues identified in the CRL. The CRL provided multiple options for resolving the identified deficiencies, including submission of the data from at least one additional adequate and well-controlled trial demonstrating the efficacy of veverimer for the treatment of metabolic acidosis associated with CKD.

We held an End-of-Review Type A meeting, or Type A meeting, with the FDA's Division of Cardiology and Nephrology, or the Division, in October 2020. The Division agreed, in principle, that an interim analysis of serum bicarbonate data from the VALOR-CKD trial proposed by Tricida could address the Division's concerns regarding the reliability of the TRCA-301/TRCA-301E trial data and the relevance of those trial findings to the U.S. population provided certain conditions were met. Based on other feedback from the FDA during the Type A meeting, we believed the Division would also require evidence of veverimer's effect on CKD progression from a near-term interim analysis of the VALOR-CKD trial for accelerated approval and that the FDA would be unlikely to rely solely on serum bicarbonate data for determination of efficacy. Accordingly, we submitted a Formal Dispute Resolution Request, or FDRR, solely requesting that the Office of New Drugs, or OND, find that the magnitude of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis associated with CKD and that it can therefore serve as the basis for accelerated approval.

In February 2021, the OND issued a decision on our FDRR. While the OND acknowledged that the TRCA-301 and TRCA-301E trials met their serum bicarbonate endpoints with statistical significance, the OND denied the appeal. In its Appeal Denied Letter, or ADL, the OND not only addressed the issue of magnitude of serum bicarbonate change, but cited all of the deficiencies in the CRL in concluding that the data provided in support of the veverimer NDA did not support approval through the Accelerated Approval Program. The OND concluded that the magnitude of the increases in serum bicarbonate levels shown in the TRCA-301/TRCA-301E trial was not of sufficient size or duration to establish that treatment with veverimer would be reasonably likely to provide a discernible reduction in CKD progression. In addition, the OND found that the intended confirmatory trial, VALOR-CKD (also known as TRCA-303), was underpowered to detect a 13% reduction in slowing of CKD progression. This finding was based on information included in the initial NDA submission, including the placebo-subtracted LS mean change from baseline in serum bicarbonate observed in the TRCA-301/TRCA-301E trial and the original Predictive MA Model. The OND also raised concerns regarding the robustness of the study results given that the veverimer

NDA was supported by a single registrational trial (TRCA-301/TRCA-301E), which must, alone, provide persuasive evidence of benefit. Specifically, the OND noted concerns around adequate blinding, the trial results being strongly influenced by a single site, and the majority of sites for the TRCA-301/TRCA-301E trial being in Eastern Europe, where differences in patient management, including concomitant medications and diet, might affect the treatment response to veverimer and raise a concern of the applicability to a U.S. patient population. The OND also stated that, while trial results in the TRCA-301/TRCA-301E trial showed improvement in two patient-reported measures, the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test, the OND viewed this subjective data from a single trial with skepticism in the absence of data from a second trial with similar results and noted that both endpoints would require rigorous blinding to support robust conclusions. However, the OND noted that both of these changes, if eventually established by one or more additional trials, would indicate a potentially meaningful benefit of veverimer treatment—especially in CKD patients who have physical functional impairments. Separate from the ADL, we previously received feedback from the Division of Clinical Outcome Assessment, or DCOA, that reliance on these physical function endpoints for approval may require further validation.

Based on the ADL, we believe that we now have greater clarity on the potential approval of veverimer through the Accelerated Approval Program. The OND suggested that we meet with the Division to discuss submission of Week 52 serum bicarbonate results from the full randomized trial population of VALOR-CKD and that the trial should include a substantial portion of patients from the United States or from regions with "US-like" patients. If the results of this trial were to demonstrate that veverimer provides a meaningfully larger treatment effect than seen in the TRCA-301/TRCA-301E trial, then this trial, along with the results from the TRCA-301/TRCA-301E trial, could address the concerns raised in the CRL regarding the limitations and the size of the treatment response observed in the TRCA-301/TRCA-301E trial. However, whether the extent of increase in serum bicarbonate in any subsequent submission based on VALOR-CKD would support accelerated approval will remain a review issue, and will, in part, reflect the Division's assessment of the adequacy (i.e., power) of VALOR-CKD to detect the anticipated treatment effect of CKD progression in a reasonable timeframe.

Although the ADL provides greater clarity on the potential path for approval of veverimer through the Accelerated Approval Program, we believe the timeline to meet the requirements for accelerated approval as suggested in the ADL may not result in the most rapid development path for veverimer. For example, if either of the planned interim analyses in VALOR-CKD for early stopping for efficacy results in positive renal outcomes data, this data could be available before the week 52 serum bicarbonate data from the fully enrolled VALOR-CKD trial suggested in the ADL and could serve as the basis for resubmission of the NDA. We are evaluating several options with respect to the VALOR-CKD trial that are focused on obtaining, prior to the end of 2022, additional data on the effect of veverimer on (1) CKD progression; (2) physical functioning; and (3) serum bicarbonate. We may explore the possibility of stopping the trial early for administrative reasons, which would allow analysis of the data using all alpha remaining at that time. In any event, we believe data from VALOR-CKD will be very important in furthering our understanding of the regulatory path for approval of veverimer. As such, we intend to continue the execution of the VALOR-CKD trial with consideration of both the accelerated and traditional approval pathways. Resubmission of the veverimer NDA may require additional clinical data beyond that provided by the VALOR-CKD trial, including an additional trial or trials to confirm magnitude, durability of effect or applicability to the U.S. population.

Even if we obtain regulatory approval for veverimer, we will need to develop a commercial organization, or collaborate with a third party for the commercialization of veverimer, establish commercially viable pricing and obtain approval for coverage and adequate reimbursement from third parties, including government payers. If we are unable to successfully commercialize veverimer, we may not be able to generate sufficient revenue to continue our business.

Our near-term prospects, including our ability to finance our operations and generate revenue, will depend heavily on the successful development, regulatory approval and commercialization of veverimer in the United States. Though we plan to engage in marketing approval discussions with foreign regulatory agencies in the future, we have not yet begun marketing approval discussions with any regulatory agency other than the FDA, and we are not currently seeking regulatory approval for veverimer outside the United States. The clinical and commercial success of veverimer will depend on a number of factors, including the following:

- our ability to demonstrate veverimer's safety and efficacy to the satisfaction of the FDA and/or foreign regulatory agencies;
- the timely reporting of our ongoing VALOR-CKD trial;

- our ability to conduct a successful VALOR-CKD trial and the ability of the results of this trial to demonstrate clinical benefit if we seek traditional approval of veverimer or confirm clinical benefit if we obtain accelerated approval of veverimer;
- the enrollment and continued participation in our VALOR-CKD trial by a sufficient number of subjects to demonstrate applicability to the U.S. population;
- the enrollment and continued participation in our VALOR-CKD trial by a sufficient number of subjects over a sufficient number of clinical sites to avoid the potential for trial results to be driven by a single high-enrolling site;
- whether we are required by the FDA and/or foreign regulatory agencies to conduct additional clinical trials prior to or after approval to market veverimer, in addition to our VALOR-CKD trial;
- the prevalence and severity of adverse side effects of veverimer in our ongoing and future clinical trials and commercial use, if approved;
- the timely receipt of necessary regulatory and marketing approvals from the FDA and/or foreign regulatory agencies for veverimer;
- our ability to obtain U.S. marketing approval for veverimer through the Accelerated Approval Program or traditional approval process, including our ability to address any deficiencies identified by the FDA in the CRL or issues identified in the ADL issued by the OND on our FDRR;
- our ability to successfully commercialize veverimer, if approved for marketing and sale by the FDA and/or foreign regulatory agencies;
- our ability to manufacture clinical trial and commercial quantities of veverimer drug substance and drug product and to develop and maintain commercially viable and validated manufacturing processes that are compliant with current good manufacturing practices, or cGMP, at a scale sufficient to meet anticipated demand and over time enable us to reduce our cost of manufacturing;
- achieving and maintaining compliance with all regulatory requirements applicable to veverimer;
- our success in educating physicians and patients about the potential benefits, risks, administration and use of veverimer;
- acceptance of veverimer as safe and effective by patients and the medical community;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;
- our ability to obtain and sustain an adequate level of reimbursement for veverimer by third-party payers;
- the effectiveness of our own or any future strategic collaborators' marketing, sales and distribution strategy and operations;
- our ability to continue to obtain protection for and to enforce our intellectual property rights in and to veverimer;
- the impact of pandemics, such as COVID-19, on our business; and
- our ability to avoid and defend against third-party patent interference or patent infringement claims or similar proceedings with respect to our patent rights and patent infringement claims.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of veverimer. If we are not successful in gaining approval of or in commercializing veverimer, or are significantly delayed in doing so, our business will be materially harmed.

If we are unable to obtain approval of veverimer through the Accelerated Approval Program in the United States, and/or are required to conduct additional nonclinical and clinical studies and trials beyond those that

we have completed or currently contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approval. Even if we receive approval from the FDA through the Accelerated Approval Program, if the ongoing VALOR-CKD trial, which would serve as a confirmatory postmarketing trial, or any additional confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous postmarketing requirements, the FDA may seek to withdraw the approval.

As described in the "Government Regulation" section, the Accelerated Approval Program is one of several approaches used by the FDA to make prescription drugs more rapidly available for the treatment of serious or life-threatening diseases. The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides a meaningful advantage over available therapies upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, which, is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. Approval through the Accelerated Approval Program is subject, however, to the requirement that the applicant conduct at least one additional confirmatory postmarketing clinical trial to verify and describe the drug's clinical benefit, where there is uncertainty as to the relationship of the surrogate endpoint to the clinical benefit, or of the observed clinical endpoint to ultimate outcome. Typically, clinical benefit is verified when a postmarketing clinical trial shows that the drug provides a clinically meaningful positive therapeutic effect, that is, an effect on how a patient feels, functions, or survives. If such confirmatory postmarketing trial fails to confirm the drug's clinical profile or risks and benefits, the FDA may withdraw its approval of the drug.

The FDA has broad discretion with regard to approval through the Accelerated Approval Program, and even if we believe that the Accelerated Approval Program is appropriate for veverimer, we cannot assure you that the FDA will ultimately agree. Furthermore, even if we do obtain approval through the Accelerated Approval Program, we may not experience a faster development process, review or approval compared to the traditional approval process.

Our NDA for veverimer was reviewed by the FDA through the Accelerated Approval Program based on the results of our Phase 1/2 trial, TRCA-101, our Phase 3 clinical trial, TRCA-301, and our 40-week extension trial, TRCA-301E. Thus far, we have been unable to obtain approval of veverimer through the Accelerated Approval Program. In August 2020, we received a CRL from the FDA related to our NDA for veverimer. According to the CRL, the FDA is seeking additional data beyond the TRCA-301/TRCA-301E trial regarding the magnitude and durability of the treatment effect of veverimer on the surrogate marker of serum bicarbonate and expressed concern regarding whether the demonstrated effect size would be reasonably likely to predict clinical benefit. In addition, the CRL questioned the applicability of the treatment effect to the U.S. population and the practice of medicine in the United States. The FDA also expressed concern as to the reliability of the findings given that the findings for the TRCA-301/TRCA-301E trial were driven by a single, high-enrolling trial site located in Eastern Europe. The CRL did not raise any concerns related to FDA's completed inspection of the highest enrolling clinical trial site in the TRCA-301/TRCA-301E trial and there was no FDA Form 483 issued. There were no safety, clinical pharmacology/ biopharmaceutics, CMC, or non-clinical issues identified in the CRL. The CRL provided multiple options for resolving the identified deficiencies, including submission of the data from at least one additional adequate and well-controlled trial demonstrating the efficacy of veverimer for the treatment of metabolic acidosis associated with CKD.

We held an End-of-Review Type A meeting, or Type A meeting, with the FDA's Division of Cardiology and Nephrology, or the Division, in October 2020. The Division agreed, in principle, that an interim analysis of serum bicarbonate data from the VALOR-CKD trial proposed by Tricida could address the Division's concerns regarding the reliability of the TRCA-301/TRCA-301E trial data and the relevance of those trial findings to the U.S. population provided certain conditions were met. Based on other feedback from the FDA during the Type A meeting, we believed the Division would also require evidence of veverimer's effect on CKD progression from a near-term interim analysis of the VALOR-CKD trial for accelerated approval and that the FDA would be unlikely to rely solely on serum bicarbonate data for determination of efficacy. Accordingly, we submitted a Formal Dispute Resolution Request, or FDRR, solely requesting that the Office of New Drugs, or OND, find that the magnitude of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis associated with CKD and that it can therefore serve as the basis for accelerated approval.

In February 2021, the OND issued a decision on our FDRR. While the OND acknowledged that the TRCA-301 and TRCA-301E trials met their serum bicarbonate endpoints with statistical significance, the OND denied the appeal. In its Appeal Denied Letter, or ADL, the OND not only addressed the issue of magnitude of serum bicarbonate change, but cited all of the deficiencies in the CRL in concluding that the data provided in support of the veverimer NDA did not support approval through the Accelerated Approval Program. The OND concluded that the magnitude of the increases in serum bicarbonate levels shown in the TRCA-301/TRCA-301E trial was not of sufficient size or duration to establish that treatment with veverimer would be reasonably likely to provide a discernible reduction in CKD progression. In addition, the OND found that the intended confirmatory trial, VALOR-CKD (also known as TRCA-303), was underpowered to detect a 13% reduction in slowing of CKD progression. This finding was based on information included in the initial NDA submission, including the placebo-subtracted LS mean change from baseline in serum bicarbonate observed in the TRCA-301/TRCA-301E trial and the original Predictive MA Model. The OND also raised concerns regarding the robustness of the study results given that the veverimer NDA was supported by a single registrational trial (TRCA-301/TRCA-301E), which must, alone, provide persuasive evidence of benefit. Specifically, the OND noted concerns around adequate blinding, the trial results being strongly influenced by a single site, and the majority of sites for the TRCA-301/TRCA-301E trial being in Eastern Europe, where differences in patient management, including concomitant medications and diet, might affect the treatment response to veverimer and raise a concern of the applicability to a U.S. patient population. The OND also stated that, while trial results in the TRCA-301/TRCA-301E trial showed improvement in two patient-reported measures, the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test, the OND viewed this subjective data from a single trial with skepticism in the absence of data from a second trial with similar results, and noted that both endpoints would require rigorous blinding to support robust conclusions. However, the OND noted that both of these changes, if eventually established by one or more additional trials, would indicate a potentially meaningful benefit of veverimer treatment—especially in CKD patients who have physical functional impairments. Separate from the ADL, we previously received feedback from the Division of Clinical Outcome Assessment, or DCOA, that reliance on these physical function endpoints for approval may require further validation.

Based on the ADL, we believe that we now have greater clarity on the potential approval of veverimer through the Accelerated Approval Program. The OND suggested that we meet with the Division to discuss submission of Week 52 serum bicarbonate results from the full randomized trial population of VALOR-CKD and that the trial should include a substantial portion of patients from the United States or from regions with “US-like” patients. If the results of this trial were to demonstrate that veverimer provides a meaningfully larger treatment effect than seen in the TRCA-301/TRCA-301E trial, then this trial, along with the results from the TRCA-301/TRCA-301E trial, could address the concerns raised in the CRL regarding the limitations and the size of the treatment response observed in the TRCA-301/TRCA-301E trial. However, whether the extent of increase in serum bicarbonate in any subsequent submission based on VALOR-CKD would support accelerated approval will remain a review issue, and will, in part, reflect the Division’s assessment of the adequacy (i.e., power) of VALOR-CKD to detect the anticipated treatment effect of CKD progression in a reasonable timeframe.

Although the ADL provides greater clarity on the potential path for approval of veverimer through the Accelerated Approval Program, we believe the timeline to meet the requirements for accelerated approval as suggested in the ADL may not result in the most rapid development path for veverimer. For example, if either of the planned interim analyses in VALOR-CKD for early stopping for efficacy results in positive renal outcomes data, this data could be available before the week 52 serum bicarbonate data from the fully enrolled VALOR-CKD trial suggested in the ADL and could serve as the basis for resubmission of the NDA. We are evaluating several options with respect to the VALOR-CKD trial that are focused on obtaining, prior to the end of 2022, additional data on the effect of veverimer on (1) CKD progression; (2) physical functioning; and (3) serum bicarbonate. We may explore the possibility of stopping the trial early for administrative reasons, which would allow analysis of the data using all alpha remaining at that time. In any event, we believe data from VALOR-CKD will be very important in furthering our understanding of the regulatory path for approval of veverimer. As such, we intend to continue the execution of the VALOR-CKD trial with consideration of both the accelerated and traditional approval pathways. Resubmission of the veverimer NDA may require additional clinical data beyond that provided by the VALOR-CKD trial, including an additional trial or trials to confirm magnitude, durability of effect or applicability to the U.S. population.

Because we may continue to develop our investigational drug candidate for the treatment of a disease or condition on the basis of an unvalidated surrogate endpoint, there are increased risks that the FDA may have difficulty analyzing and interpreting the results of our clinical program. In addition, the FDA may find that the demonstrated effect on a surrogate endpoint is not reasonably likely to predict clinical benefit. As a result, they may delay or refuse to approve veverimer. We have engaged in discussions with the FDA regarding the design of our Phase 3 clinical trial, TRCA-301/TRCA-301E, and whether the use of serum bicarbonate as a surrogate endpoint is reasonably likely to predict clinical benefit. While the FDA has agreed in principle that serum bicarbonate may be an acceptable surrogate endpoint, the FDA has not set forth the minimum change in serum bicarbonate that it believes would be reasonably likely to predict clinical benefit.

If we are able to obtain accelerated approval for veverimer , we will be subject to rigorous postmarketing requirements, including the completion of our ongoing VALOR-CKD trial, which we believe would serve as a confirmatory postmarketing trial, or such other confirmatory trials as the FDA may require, to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw the approval for multiple reasons, including if we fail to conduct any required postmarketing trial with due diligence, our confirmatory postmarketing trial does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false and misleading.

There can be no assurance that data from VALOR-CKD can be obtained on a timely basis or that they will be sufficient to support approval of veverimer. Any further delay in obtaining, or inability to obtain, approval would delay or prevent commercialization of veverimer and would materially adversely affect our business, financial condition, results of operations, cash flows and prospects. The denial of regulatory approval for veverimer could mean that we need to cease operations altogether.

We may be unable to obtain regulatory approval for veverimer under the traditional FDA approval process.

We may decide to pursue traditional approval of veverimer for the treatment of metabolic acidosis and slowing of kidney disease progression or improving physical functioning in patients with metabolic acidosis associated with CKD rather than accelerated approval. To obtain traditional approval to market a drug product, we must provide the FDA with clinical data that adequately demonstrate the safety and efficacy of veverimer for the intended indication sought in the NDA.

The FDA generally requires at least two adequate and well-controlled studies to support approval of an NDA. A single Phase 3 clinical trial may be sufficient in rare instances, including (1) where the clinical trial is a large multicenter clinical trial demonstrating internal consistency and a statistically persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second clinical trial would be practically or ethically impossible or (2) when in conjunction with other confirmatory evidence. If the VALOR-CKD trial is successful, and we decide to pursue traditional approval, it would be based on our belief that our VALOR-CKD trial, supported by the TRCA-301/ TRCA-301E trial, will provide sufficient evidence for FDA to approve veverimer for the treatment of metabolic acidosis and slowing of kidney disease progression or improving physical functioning in patients with metabolic acidosis associated with CKD. However, it is possible that the FDA will disagree. The FDA has broad discretion in determining whether to approve a drug, and the FDA could find a resubmitted NDA seeking traditional approval of veverimer on the basis of VALOR-CKD to be insufficient for a number of reasons, including the following reasons:

- concerns regarding the robustness of the VALOR-CKD trial results;
- concerns that the VALOR-CKD results are not generalizable to patients in the United States, including if the outcome events are driven by events in Eastern European subjects or there is an insufficient number of events in U.S. or "US-like" subjects;
- concerns that the tools used to assess our patient-reported measures, the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test, are not sufficiently validated for purposes of regulatory approval; and
- concerns that potential blinding issues could affect our trial results, including patient-reported measures, which are subjective.

If the FDA were to find that the results of our VALOR-CKD trial as supported by results from the TRCA-301/ TRCA-301E trial are inadequate for approval of veverimer, the FDA would not approve our NDA.

A delay in obtaining regulatory approval could delay commercialization of veverimer and adversely impact our ability to generate revenue, our business and our results of operations and the denial of such approval for veverimer could mean that we need to cease operations.

If we are not successful in obtaining approval to commercialize veverimer, or are significantly delayed in doing so, our business will be materially harmed, and we may need to curtail or cease operations. We are not permitted to market veverimer in the United States until we receive approval to market veverimer from the FDA. Similarly, we are not permitted to market veverimer in other countries until we receive approval to market veverimer from comparable foreign regulatory agencies.

We currently have no drug products approved for sale, and we may never obtain regulatory approval to market veverimer, either through the FDA's Accelerated Approval Program or the traditional approval process. If we are unable to address the deficiencies identified in the CRL and the concerns identified in the ADL to the satisfaction of the FDA, we will not obtain regulatory approval of veverimer.

The FDA or any foreign regulatory agency can further delay, limit or deny approval to market veverimer for many reasons, including:

- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory agency that veverimer is safe and effective for the requested indication;
- our inability to gain agreement from the FDA that veverimer is appropriate for approval through FDA's Accelerated Approval Program or through traditional approval;
- our inability to gain agreement from applicable foreign regulatory authorities that veverimer is appropriate for approval under applicable regulatory pathways;
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from nonclinical and clinical studies and trials;
- our ability to demonstrate that the results are applicable to the U.S. population or practice of medicine;
- our inability to demonstrate that the clinical and other benefits of veverimer outweigh any safety or other perceived risks;
- our ability to enroll an adequate number of subjects in a timely manner in our ongoing VALOR-CKD trial;
- the FDA's or the applicable foreign regulatory agency's requirement for additional nonclinical or clinical studies or trials;
- the FDA's or the applicable foreign regulatory agency's having differing requirements for the trial protocols used in our clinical trials;
- the FDA's or the applicable foreign regulatory agency's non-approval of the formulation, labeling and/or the specifications of veverimer;
- the FDA may require, as a condition of approval, modifications to existing, or additional, nonclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA's or the applicable foreign regulatory agency's failure to accept the manufacturing processes or third-party manufacturers with which we contract;
- the impact that pandemics, such as COVID-19, may have on the FDA's ability to review our NDA;
- the impact that pandemics, such as COVID-19, may have on our ability to enroll and retain an adequate number of subjects in or the power of our ongoing VALOR-CKD trial; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized.

Even if we eventually complete clinical testing and receive approval of our NDA or foreign marketing authorization for veverimer, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, which may be required after approval. The FDA or the applicable foreign regulatory agency may only approve veverimer subject to certain other conditions being met either before or after approval. The FDA or the applicable foreign regulatory agency may also approve veverimer for a more limited indication and/or a narrower patient population than we originally request, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of veverimer. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of veverimer and would materially adversely impact our business and prospects.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and failure can occur at any stage of clinical development.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of nonclinical and clinical studies and trials of our investigational drug candidate may not be predictive of the results of later-stage clinical trials. For example, the positive results generated to date in our Phase 1/2 trial, TRCA-101, our Phase 3 trial, TRCA-301, and our 40-week extension trial, TRCA-301E, for veverimer do not ensure that our ongoing VALOR-CKD trial, or other future clinical trials will demonstrate similar results. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through nonclinical and clinical studies and trials. Several companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies and trials, and we cannot be certain that we will not face similar setbacks. Based upon negative or inconclusive results, we or any potential future collaborator may decide, or regulators may require us, to conduct additional nonclinical and clinical studies and trials. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Additionally, clinical trials must be conducted in a manner that ensures the trial design and operations are carried out in a way that preserves double-blind placebo-controlled status and maintains clinical trial data integrity. Furthermore, we rely on contract research organizations, or CROs, and clinical trial sites to ensure the proper and timely conduct of our clinical trials and, while we have agreements governing their committed activities, we have limited influence over their actual performance. Even though we completed our registrational trial, TRCA-301/TRCA-301E, and even if any future clinical trials are completed, the results may not be sufficient to obtain regulatory approval, regardless of whether it is through the Accelerated Approval Program or the traditional approval process, for veverimer in the time frame we anticipate, or at all. Additional clinical trial results may inform our understanding of the safety and efficacy of veverimer and could impact the design and conduct of ongoing and future clinical trials.

A number of companies in the pharmaceutical industry have suffered significant setbacks in clinical trials even after promising results in earlier nonclinical or clinical studies and trials. These setbacks have been caused by, among other things, nonclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. Success in nonclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the results of clinical trials by other parties may not be indicative of the results in trials we may conduct. In addition, results from compassionate use or investigator-initiated research programs, if implemented, may not be confirmed in Company-sponsored trials and/or may negatively impact the prospects for marketing approval for veverimer.

Subject enrollment and retention are significant factors in the conduct of clinical trials and they are affected by many factors, including the size and nature of the patient population, the proximity of subjects to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and subjects' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating. The occurrence of pandemics, such as COVID-19, may negatively impact the ability to enroll, maintain and collect safety and efficacy data on subjects in a clinical trial.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the ethics committees or IRBs of the institutions in which such trials are being conducted, by an independent Data Monitoring Committee, or DMC, for such trial or by the FDA or other regulatory agencies. Such parties may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory agencies resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, conducting clinical trials in foreign countries presents additional risks that may delay completion of our clinical trials. These risks include the failure of physicians or enrolled subjects in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. In addition, the FDA may determine that clinical trial results obtained in foreign subjects do not represent the safety and efficacy of a product when administered in U.S. patients and are thus not supportive of our NDA approval in the United States. Foreign authorities may have similar reservations in accepting data from clinical trials conducted outside of their territory for future marketing approvals outside of the U.S. The CRL issued by FDA questions the applicability of the TRCA-301/TRCA-301E trial findings to the U.S. population and practice of medicine, and based on feedback received from the FDA, although we have elected to focus future enrollment activities in our ongoing VALOR-CKD trial in the United States, Canada and Western Europe, to meet our goal of completing enrollment in 2021, we may need to also enroll subjects in other non-Eastern European regions. When the VALOR-CKD trial is fully recruited, we anticipate that approximately 67% of subjects will have been enrolled at Eastern European sites and approximately 10-20% of subjects will have been enrolled at sites in the U.S., Western Europe and Canada. However, our ongoing VALOR-CKD trial may have a large dropout rate of participants, or a low event rate, which could add time, expense and risk to the completion of the trial and could affect the results of the trial.

In August 2020, we received a CRL from the FDA for our NDA for veverimer. We held an End-of-Review meeting as a Type A meeting with the FDA's Division of Cardiology and Nephrology in October 2020. Thereafter, we submitted an FDRR requesting that the OND find that the magnitude of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis associated with CKD and that it can therefore serve as the basis for accelerated approval.

In February 2021, the OND issued a decision on our FDRR. While it acknowledged that the TRCA-301 and TRCA-301E trials met their serum bicarbonate endpoints with statistical significance, the OND issued an ADL and denied the appeal. We are still considering our options regarding how to proceed. We cannot assure you that we will be able to address the deficiencies identified in the CRL and the ADL to the satisfaction of the FDA.

In addition, we do not know whether future clinical trials, if any, will begin on time, need to be redesigned, enroll an adequate number of subjects on time or be completed on schedule, if at all. Clinical trials can be delayed, terminated early or aborted for a variety of reasons, including delay or failure to:

- obtain regulatory approval to commence a trial, if applicable;
- reach agreement on acceptable terms with prospective CROs, other third-party contract service providers and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs, other third-party contract service providers and trial sites;
- obtain ethics committee or institutional review board, or IRB, approval at each site;
- recruit suitable trial subjects across an adequate number of suitable clinical trial sites and have such subjects complete the clinical trial or return for post-treatment follow-up;
- ensure that clinical sites follow the trial protocol, comply with GCP, and continue to participate in a clinical trial;
- address any subject safety concerns that arise during the course of a clinical trial;
- ensure that subjects comply with and complete clinical trial protocol;
- achieve a sufficient level of endpoint events in the placebo group, if applicable;
- initiate or add a sufficient number of clinical trial sites;
- ensure that trial sites do not deviate from clinical trial protocol or drop out of a clinical trial;
- ensure that the clinical trial design and operational integrity are conducted in a manner that preserves double-blind placebo-controlled status and maintains clinical trial data integrity;
- address any conflicts with new or existing laws or regulations;
- manufacture sufficient quantities of drug candidate for use in clinical trials and ensure clinical trial material is provided to clinical sites in a timely manner;

- the impact of pandemics, such as COVID-19; and
- obtain the statistical analysis plan to be used to evaluate the clinical trial data.

If we experience delays in the start or completion of, or termination of, any clinical trial of our sole investigational drug candidate, veverimer, the commercial prospects of veverimer may be harmed, and our ability to generate product revenue from veverimer will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our veverimer development and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of veverimer.

Results from completed human clinical trials may not be representative of the results that are obtained after approval, if obtained, and product launch.

Human clinical trials are very complicated undertakings and conducting CKD trials is particularly difficult because of the serious nature of the disease and the comorbidities experienced by these patients. If we obtain FDA approval for veverimer, differences in the safety and efficacy profile not identified in our prior clinical trials may first appear after we obtain approval and commercialize veverimer. For example, any new postmarketing adverse events may significantly impact our ability to market veverimer and may require that we make changes to the product label that could adversely impact our commercialization efforts, recall some or all of the product, or discontinue commercialization of the product. Furthermore, if we are able to obtain accelerated approval of veverimer and if the ongoing VALOR-CKD trial fails to confirm veverimer's clinical profile or clinical benefits, the FDA may withdraw its approval of veverimer. Any of these events would materially harm our business.

We have relied and continue to rely on third parties, particularly CROs, to conduct and complete our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize veverimer, if approved.

We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, contract laboratories, collaborative partners and other third parties, such as CROs, to conduct clinical trials for veverimer. We rely on these third parties to conduct and complete our clinical trials according to GCP and the trial protocol, statistical analysis plan and other trial-specific documents (for example, safety management, clinical monitoring and blinding plans). Responsibilities of these third parties include, but are not limited to, monitoring of the trial sites and ensuring that the trial is conducted in compliance with International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, or ICH, guidelines and GCP, the informed consent process, protocol-specified requirements, safety reporting requirements, data collection guidelines and all trial-specific blinding procedures.

The third parties with whom we contract for execution of our clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and, except for contractual duties and obligations, we have limited ability to control the amount or timing of resources that they devote to our program. Although we rely on these third parties to conduct all of our clinical trials in accordance with a transfer of obligations, we remain responsible for ensuring that each of our clinical trials is conducted and its data analyzed in accordance with its protocol and statistical analysis plan. Moreover, the FDA and foreign regulatory agencies require us to comply with regulations and standards, including ICH guidelines and 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 subjects are adequately informed of the potential risks of participating in clinical trials.

In addition, the execution of clinical trials, and the subsequent compilation and analysis of the data produced, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. Moreover, these third parties may also have relationships with other commercial entities, some of which may compete with us. These third parties may terminate their agreements with us upon as little as 30 days' prior written notice. Some of these agreements may also be terminated by such third parties under certain other circumstances, including our insolvency. If the third parties conducting our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the intentional or inadvertent failure to adhere to our clinical trial protocols or GCP, or for any other reason, we may need to enter into new arrangements with alternative third parties, which could be difficult, costly or impossible, and our clinical trials may be extended, delayed or terminated or may need to be repeated. The third parties upon whom we rely may be inspected by FDA or other regulatory authorities in relation to our, or to other, studies or trials. Such inspections may be impacted by pandemics, such as COVID-19, and/or may result in FDA or other regulatory authorities not accepting the data produced by the third party.

If any of the foregoing were to occur, we may not be able to obtain regulatory approval for or commercialize veverimer, which would have a material adverse effect on our business, results of operations and financial condition.

We rely completely on third-party suppliers to manufacture, package and label our clinical drug supply of veverimer drug substance and drug product, and we intend to rely on third parties to produce, package and label commercial supply of veverimer drug substance and drug product, if approved.

We do not currently have, nor do we plan to acquire, the infrastructure or internal capability to manufacture, package and label veverimer on a clinical or commercial scale. As such, we contract with third-party service providers to manufacture veverimer drug substance and drug product, to perform analytical testing services and to package and label the product under cGMPs. Pharmaceutical manufacturing, testing and packaging facilities are subject to inspection by the FDA and foreign regulatory agencies on a regular basis, before and after product approval.

We do not directly control, and are completely dependent on, our contract manufacturers for compliance with, applicable requirements including cGMP, for manufacture of both veverimer drug substance and drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications or that can consistently or reliably be converted into drug product and meet any other requirements of our third-party suppliers, or are unable to comply with the strict regulatory requirements of the FDA or foreign regulatory agencies, we will not be able to secure and/or maintain adequate supply of veverimer drug substance and drug product. In addition, we have no direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such other materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may generally affect the regulatory clearance of our contract manufacturers' facilities. If our contract manufacturers' facilities fail to comply with the FDA or a comparable foreign regulatory agency requirement, we may need to find alternative manufacturing facilities for veverimer drug substance or drug product, which would negatively impact our ability to develop, obtain regulatory approval for, or commercialize veverimer, if approved, and materially adversely affect our financial condition.

We currently depend on single third-party suppliers for the manufacture of veverimer drug substance and drug product, and any supply interruption in veverimer drug substance or drug product could materially harm our ability to complete our development program or satisfy commercial demand, if approved, until a new source of supply, if any, could be identified and qualified.

We cannot be certain that our drug substance supplier will continue to provide us with sufficient quantities of veverimer drug substance, or that our drug product manufacturer will be able to produce sufficient quantities of drug product incorporating such drug substance, to satisfy our anticipated specifications and quality requirements, or that such quantities can be obtained at pricing necessary to sustain acceptable pharmaceutical margins. We believe that there are a limited number of experienced contract manufacturers in the world capable of manufacturing a polymeric drug substance such as veverimer. Our current dependence on a single supplier for our drug substance and the challenges we may face in obtaining adequate supply of veverimer drug substance involves several risks, including limited control over pricing, availability, quality and delivery schedules. Any supply interruption in veverimer drug substance or drug product could materially harm our ability to complete our development program or satisfy commercial demand, if approved, until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Further, even if we were able to identify an alternative third-party supplier, such supplier would be subject to significant technical and regulatory requirements. Any performance failure on the part of our suppliers could delay the development and potential commercialization of veverimer, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Moreover, our current supplier of drug substance may not have the capacity to manufacture veverimer drug substance in the quantities that we believe will be sufficient to meet anticipated market demand or to enable us to achieve the economies of scale necessary to reduce the manufacturing cost of veverimer drug substance. We entered into a commercial supply agreement with our current drug substance supplier and are engaging in discussions with a potential second supplier for commercial drug substance. Our long-term commitment under the commercial supply agreement to purchase veverimer drug substance could create a significant financial obligation. Negotiations with a potential second supplier may not lead to a definitive agreement on acceptable terms, or at all, which could have a material adverse effect on our business. Our business plan assumes that we are able to develop a supply chain with multiple suppliers and significantly decrease our cost of goods within the first several years of commercialization of veverimer, if approved, enabling us to achieve gross margins similar to those achieved by other companies with polymer-based drugs. If we are unable to reduce the manufacturing cost of veverimer drug substance, our financial results will suffer and our ability to achieve profitability will be significantly jeopardized. Outside of our current supplier, we currently do not have any agreements for the commercial production of veverimer drug substance. If our contract manufacturer for drug substance is unable to source, or we are unable to purchase, sufficient quantities of materials necessary for the production of veverimer drug substance, the ability of veverimer to reach its market potential or to be timely launched, would be delayed or suffer from a shortage in supply, which would impair our ability to generate revenue from the sale of veverimer.

If there is a disruption to our contract manufacturers' or suppliers' relevant operations, we will have no other means of producing veverimer drug substance and drug product until they restore the affected facilities or we or they procure alternative manufacturing facilities. Additionally, any damage to or destruction of our contract manufacturers' or suppliers' facilities or equipment or the impact of a pandemic, such as COVID-19, may significantly impair our ability to manufacture veverimer on a timely basis.

Any performance failure or time delay in further optimizing or scaling our drug substance and/or drug product manufacturing processes could materially adversely affect, delay or interrupt the execution of our ongoing VALOR-CKD trial and potentially impact the commercialization of veverimer, if approved.

At this time, we believe we have sufficient drug substance and access to sufficient drug product manufacturing capacity to supply the anticipated demand of our ongoing VALOR-CKD trial. As compared to soluble, small organic molecule pharmaceuticals, insoluble, non-absorbed polymers are manufactured in larger batches to satisfy greater doses, e.g., gram quantities versus milligram or even microgram quantities per dose, which presents unique requirements both in terms of scale-up and process controls. Any difficulties experienced in the ongoing effort to further optimize and scale our drug substance and/or drug product manufacturing processes could materially adversely affect or delay our ability to (i) have sufficient quantities of veverimer drug substance and drug product manufactured to successfully conduct our ongoing VALOR-CKD trial, or (ii) have sufficient quantities of veverimer drug substance and drug product to supply commercial supply of veverimer, if approved, all of which would have a material adverse effect on our business and our prospects.

If we fail to establish an effective distribution process for veverimer drug product, if approved, our business may be adversely affected.

Once a product receives marketing approval, the manufacturing, distribution, processing, formulation, packaging, labeling, promotion and sale of pharmaceutical products are subject to extensive regulation by federal and state agencies, which are subject to change by the relevant federal, state and local agencies. For example, Title II of the Federal Drug Quality and Security Act of 2013, known as the Drug Supply Chain Security Act, or DSCSA, has imposed new "track and trace" requirements on the distribution of prescription drug products by manufacturers, distributors, and other entities in the drug supply chain. The DSCSA requires product identifiers (i.e., serialization) on prescription drug products in order to establish an electronic interoperable prescription product system to identify and trace certain prescription drugs distributed in the United States. These requirements (some of which are still being phased in) preempt state drug pedigree requirements.

We do not currently have the infrastructure necessary for distributing pharmaceutical products to patients and there is a risk that we may be unable to comply with the serialization requirements of the DSCSA within the necessary time frames. Furthermore, compliance with the DSCSA or any future federal or state electronic pedigree requirements may increase the Company's operational expenses and impose significant administrative burdens.

While we have entered into a contract with a third-party logistics company to warehouse veverimer and distribute it, the distribution network will require significant coordination with our sales, marketing, market access and finance teams. Failure to coordinate financial systems could negatively impact our ability to accurately report product revenue. If we are unable to effectively establish and manage a compliant distribution process, the commercial launch and sales of veverimer, if approved, will be delayed or severely compromised and our results of operations may be harmed.

Even if veverimer obtains regulatory approval, it may never achieve market acceptance or commercial success, which will depend, in part, upon the degree of acceptance among physicians, patients, third-party payers and the medical community.

Even if we obtain FDA or other regulatory approvals, veverimer may not achieve market acceptance among physicians, patients, third-party payers or the medical community, and may not be commercially successful. If approved, market acceptance of veverimer depends on a number of factors, including:

- the efficacy of the product as demonstrated in clinical trials;
- the prevalence and severity of any side effects and overall safety profile of the product;
- the clinical indications for which the product is approved;
- the potential and perceived advantages of veverimer over current options or future alternative treatments;
- the effectiveness of our commercial organization and distribution channels;
- the quality of our relationships with patient advocacy groups;
- the availability and sufficiency of third-party coverage and reimbursement;
- acceptance by physicians, major operators of clinics and patients of the product as a safe and effective chronic daily treatment and willingness of physicians to prescribe veverimer;
- the cost of treatment in relation to alternative treatments and willingness to pay for veverimer, if approved, on the part of patients;
- relative convenience and ease of administration of veverimer;
- the impact of pandemics, such as COVID-19, on physician prescribing habits and patient prescription fulfillment and dosing compliance; and
- the availability of the product and our ability to meet market demand, including providing a reliable supply for long-term daily treatment.

Any failure by our investigational drug candidate, if it obtains regulatory approval, to achieve market acceptance or commercial success would adversely affect our results of operations.

The incidence and prevalence of the target patient population for veverimer are based on estimates and third-party sources. If the market opportunity for veverimer is 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 might be materially and adversely affected.

Periodically, we make estimates regarding the incidence and prevalence of target patient populations based on various third-party sources and internally generated analysis. These estimates may be inaccurate or based on imprecise data. For example, the total addressable market opportunity for veverimer will depend on, among other things, acceptance of veverimer by the medical community and patient access, drug pricing and reimbursement. The number of patients in the addressable markets may turn out to be lower than expected, patients may not be otherwise amenable to treatment with veverimer, or new patients may become increasingly difficult to identify or gain access to, all of which may significantly harm our business, financial condition, results of operations and prospects.

Veverimer, if approved, may face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration.

While we are not aware of any therapies approved by the FDA for the chronic treatment of metabolic acidosis and we are aware that AstraZeneca is conducting a clinical trial to explore the use of sodium zirconium cyclosilicate in patients with hyperkalemia and metabolic acidosis associated with chronic kidney disease. The pharmaceutical market is highly competitive and dynamic, and is characterized by rapid and substantial technological development and product innovations. Our veverimer development program may serve as a template for a fast follower to develop a competing drug candidate. Furthermore, we expect veverimer to compete against non-approved options for increasing serum bicarbonate levels, including oral alkali supplementation such as sodium bicarbonate, sodium citrate or potassium citrate. Veverimer may not be able to compete effectively with existing non-approved options for increasing serum bicarbonate levels or new drugs that may be developed by competitors. The risk of competition is specifically important to us because veverimer is our only investigational drug candidate.

Our competitors may have materially greater financial, manufacturing, marketing, research and drug development resources than we do. Large pharmaceutical companies in particular, may have extensive expertise in nonclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors.

Failure to compete effectively against available options for raising serum bicarbonate levels or in the future with new products would materially harm our business, financial condition and results of our operations.

We currently have no commercial capabilities. If we are unable to establish effective commercial capabilities or if we are unable to enter into agreements with third parties to commercialize veverimer, we may not be able to effectively generate product revenue.

We currently have no commercial capabilities. In order to commercialize veverimer, if approved, we must build marketing and sales capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If veverimer is approved by the FDA, we plan to initially commercialize it in the United States through the deployment of specialty account managers who will target that subset of nephrologists most focused on treating patients with CKD. Building the requisite sales, marketing and distribution capabilities will be expensive and time-consuming and will require significant attention of our leadership team to manage. Any failure or delay in the development of our sales, marketing or distribution capabilities would adversely impact the commercialization of our product. The competition for talented individuals experienced in selling and marketing pharmaceutical products is intense, and we cannot assure you that we can assemble and retain an effective team. Additionally, we may choose to collaborate, either globally or on a territory-by-territory basis, with third parties on the commercialization of veverimer. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize veverimer if and when it receives regulatory approval or any such commercialization may experience delays or limitations.

We may be subject to additional risks related to operating in foreign countries either ourselves or through a third party, including:

- differing regulatory requirements in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- 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 United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign anti-corruption laws and regulations;

- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or health crises.

Our clinical development program may not uncover all possible adverse events that patients who take veverimer may experience. The number of subjects exposed to veverimer treatment and the average exposure time in the clinical development program may be inadequate to detect adverse events, or chance findings, that may only be detected once veverimer is administered to more patients and for greater periods of time.

Clinical trials, by their nature, utilize a sample of the potential patient population. However, with a limited number of subjects and limited duration of exposure, we cannot be fully assured that veverimer has no serious or severe side effects, and any such side effects may only be uncovered with a significantly larger number of patients exposed to the drug candidate. It is possible that ongoing and future clinical trials, as well as reports received from compassionate use or investigator-initiated research programs, or veverimer used commercially, if approved, may identify safety concerns.

Although we have monitored the subjects in our trials for certain safety concerns and we have not seen evidence of significant safety concerns in our clinical trials to date, patients treated with veverimer may experience adverse reactions. The most commonly reported adverse effects experienced by more patients on veverimer than placebo in the TRCA-101 and TRCA-301/TRCA-301E trials combined were mild to moderate diarrhea and flatulence. It is possible that the FDA may ask for additional data regarding such matters. In addition, patients with CKD often experience significant and frequent comorbidities and are being treated with other medications. Although in vitro studies and human drug-drug interaction, or DDI, studies available to date indicate that veverimer does not interact with medications commonly used by patients with CKD, if significant DDIs occur in the future, veverimer may no longer be compatible with some of the medications used to treat patients with CKD. If safety problems occur or are identified after veverimer reaches the market, the FDA may require that we amend the labeling of veverimer, recall veverimer, or even withdraw approval for veverimer.

The FDA may not agree that the safety of veverimer has been sufficiently characterized by the amount and quality of data provided from our clinical development program.

The NDA safety database for new drugs intended for chronic use in non-life-threatening conditions typically includes at least 1,500 individuals, with at least 100 patients exposed to the drug for a minimum of one year (Guideline for Industry ICH-E1A: *The Extent of Population Exposure to Assess Clinical Safety: For Drugs Intended for Long-term Treatment of Non-Life-Threatening Conditions*). At the time of submitting our NDA in August 2019, the veverimer safety database was significantly smaller than the guidance suggests. Given the toxicology study results and clinical safety profile observed to date for veverimer, as well as the non-absorbed nature of the drug, we believed our proposed safety database was adequate for the FDA to file the veverimer NDA and review it under the Accelerated Approval Program, which the FDA did. In August 2020, we received a CRL from the FDA related to our NDA for veverimer. According to the CRL, if and when the Company resubmits its NDA for veverimer, it should include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b), including updated data from all nonclinical and clinical studies/trials of veverimer, as available.

Our investigational drug candidate, veverimer, may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval, reduce the commercial attractiveness of a prescribing label or result in significant negative consequences following regulatory approval, if approved.

Clinical studies of veverimer could reveal a high and unacceptable incidence and severity of undesirable and currently unknown side effects. Undesirable side effects could adversely affect patient enrollment in clinical studies, cause us or regulatory authorities to interrupt, delay or halt clinical studies result in a negative opinion by the European Medicines Agency, or EMA, the UK Medicines and Healthcare products Regulatory Agency, or MHRA, or result in the delay, denial or withdrawal of regulatory approval by the FDA, the European Commission or other global regulatory authorities. Undesirable side effects also could result in regulatory authorities mandating additional clinical testing prior to approval, postmarketing testing following approval, the implementation of risk minimization measures or a more restrictive prescribing label for a product, which, in turn, could limit the market acceptance of the product by physicians and consumers.

Drug-related side effects could result in potential product liability claims, especially if they were not included in the consent forms for clinical trials, including trials conducted under compassionate use or investigator-initiated research programs, or were not included in the warnings of any FDA-approved labeling. We currently carry product liability insurance covering use in our clinical trials in the amount of $20.0 million in the aggregate; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts if liability and legal costs exceed the threshold limits. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations, business and financial condition, and commercial reputation. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, increased costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators or other governmental entities, monetary awards to patients or other claimants, the inability to commercialize veverimer and decreased demand for our product, if approved for marketing.

Additionally, if veverimer receives regulatory approval, and we or others later identify undesirable side effects or unanticipated adverse events caused by such product, a number of potentially significant negative consequences could result, including but not limited to:

- the requirement of additional warnings on the prescribing label;
- the withdrawal of approvals by regulatory authorities;
- the requirement of a risk evaluation and mitigation strategy plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers and/or other elements to assure safe use;
- litigation and the potential to be held liable for harm caused to patients; and
- an adverse effect on our reputation.

Any of these events could prevent us from achieving or maintaining market acceptance of veverimer and could significantly harm our business, results of operations, financial condition and prospects.

If we fail to attract and keep senior management and other key personnel we may be unable to successfully develop veverimer, manufacture drug substance and drug product, conduct our clinical trials, obtain regulatory approval and commercialize veverimer, if approved.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified personnel. In particular, we are highly dependent upon our experienced senior management and other key personnel. The loss of services of any of these individuals or our inability to attract and retain additional qualified personnel could delay or prevent the successful development of our product, completion of our planned clinical trials or the commercialization of veverimer. Although we have entered into employment agreements with our senior management team, these agreements do not provide for a fixed term of service. Any of our employees could leave our employment at any time, with or without notice. As such, an extended delay in the approval of veverimer could impact our ability to attract and retain qualified senior management and other key personnel.

Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense due to the limited number of individuals who possess the skills and experience required by our industry. Further, an extended delay in the approval of veverimer could impact our ability to attract and retain qualified personnel. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

We may hire part-time employees or use consultants. As a result, certain of our employees, officers, directors or consultants may not devote all of their time to our business, and may from time to time serve as employees, officers, directors and consultants of other companies.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct 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 misconduct or other failure to be in compliance with applicable laws or regulations.

Misconduct by our employees, independent contractors, consultants, commercial partners and vendors could include intentional failures to comply with the FDA or international regulations, provide accurate information to the FDA or other international regulatory bodies, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data timely, completely and accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, 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. Misconduct by third parties could also involve the improper use of information obtained in the course of clinical trials.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from government-funded healthcare programs, such as Medicare and Medicaid, additional integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings 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.

If we seek and obtain approval to commercialize veverimer outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If veverimer is approved for commercialization outside the United States, we may enter into agreements with third parties to market veverimer outside the United States. We expect that we will be subject to additional risks related to entering into these international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems, and different competitive drugs indicated to treat metabolic acidosis;
- 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;
- workforce uncertainty in countries where labor unrest is more common than in the United States;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, natural disasters or national, regional, or global healthcare crises.

Our Term Loan contains restrictions that limit our flexibility in operating our business.

Our Loan and Security Agreement, or Term Loan, entered into with Hercules Capital Inc., or Hercules, contains various covenants that limit our ability to engage in specified types of transactions without obtaining prior consent from our lenders. These covenants limit our ability to, among other things:

- use all of our cash;
- create, incur, assume, guarantee or be or remain liable with respect to any indebtedness;
- prepay any indebtedness;
- subject our assets that serve as collateral under the loan agreement, our intellectual property and all other property and assets used in our business to any lien or legal process;
- acquire, own or make investments;
- repurchase or redeem shares of our capital stock;
- declare or pay any cash dividends or make any other cash distributions;
- lend money to our employees, officers or directors, or guarantee such loans;
- waive, release or forgive indebtedness owed by our employees, officers or directors;
- voluntarily or involuntarily transfer, sell, lease, license, lend or convey our assets;
- merge or consolidate with another business organization;
- change our corporate name, legal form or jurisdiction of formation;
- suffer a change in control;
- relocate our chief executive office or principal place of business;
- maintain deposit accounts or securities accounts without account control agreements in place; and
- limit the extension of further credit prior to the approval of the NDA for veverimer.

The covenants in our Term Loan may limit our ability to take certain actions and, in the event that we breach one or more covenants, the agent may, and at the direction of the lenders will, declare an event of default and require that we immediately repay all amounts outstanding, plus penalties and interest, terminate their commitments to extend further credit and foreclose on the collateral granted to them to secure such indebtedness. The exercise of remedies by the lenders would have a material adverse effect on our business, operating results and financial condition.

Our debt obligations expose us to risks that could adversely affect our business, operating results, overall financial condition and may result in further dilution to our stockholders.

Our Term Loan with Hercules obligates us to make certain interest and principal payments. In addition, in May 2020, we issued $200.0 million aggregate principal amount of 3.50% convertible senior notes due 2027, or Convertible Senior Notes, pursuant to which we pay interest semiannually in arrears at a rate of 3.50% per year. The Convertible Senior Notes mature on May 15, 2027, unless earlier repurchased, redeemed or converted and are not redeemable prior to May 20, 2024. Our ability to make payments on our indebtedness depends on our ability to generate cash in the future. We expect to experience negative cash flow for the foreseeable future as we fund our operations and capital expenditures. There can be no assurance we will be in a position to repay these indebtedness when due or obtain extensions to the maturity date of the Term Loan. We anticipate that we will need to secure additional funding to repay these obligations when due. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If that additional funding involves the sale of equity securities or additional convertible securities, it would result in the issuance of additional shares of our capital stock, which would result in dilution to our stockholders.

This level of debt could have an adverse impact on our business or operations. For example, it could:

- limit our flexibility in planning for the development, clinical testing, approval and marketing of veverimer;
- place us at a competitive disadvantage compared to any of our competitors that are less leveraged than we are;
- increase our vulnerability to both general and industry-specific adverse economic conditions; and
- limit our ability to obtain additional funds.

Transactions relating to our Convertible Senior Notes may dilute the ownership interest of our stockholders.

The conversion of some or all of our outstanding Convertible Senior Notes would dilute the ownership interests of existing stockholders to the extent we deliver shares upon conversion of any such Convertible Senior Notes. If the Convertible Senior Notes become convertible under the terms of the indenture governing the Convertible Senior Notes, and if holders subsequently elect to convert the Convertible Senior Notes, we could be required to deliver to them a significant number of shares of our common stock. Any sales in the public market of the common stock issuable upon conversion could adversely affect prevailing market prices for our common stock. In addition, the existence of the Convertible Senior Notes may encourage short selling by market participants because the conversion of the Convertible Senior Notes could be used to satisfy short positions. Additionally, anticipated conversion of such Convertible Senior Notes into shares of our common stock could depress the price of our common stock.

The conditional conversion feature of the Convertible Senior Notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the Convertible Senior Notes is triggered, holders of Convertible Senior Notes will be entitled to convert the Convertible Senior Notes at any time during specified periods at their option. If one or more holders elect to convert their Convertible Senior Notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their Convertible Senior Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the Convertible Senior Notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

The accounting method for convertible indebtedness securities that may be settled in cash, such as the Convertible Senior Notes, could have a material effect on our reported financial results.

Accounting Standards Codification Subtopic 470-20, or ASC 470-20, *Debt – Debt with Conversion and Other Options*, requires an entity to separately account for the liability and equity components of convertible indebtedness instruments (such as the Convertible Senior Notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects our non-convertible indebtedness interest rate. Accordingly, the equity component of the Convertible Senior Notes is required to be included in the additional paid-in capital section of stockholders' equity on our balance sheet at the issuance date, and the value of the equity component is treated as original issue discount for purposes of accounting for the indebtedness component of the Convertible Senior Notes. As a result, we will be required to recognize a greater amount of non-cash interest expense in our statement of operations and comprehensive loss in the current and future periods presented as a result of the amortization of the discounted carrying value of the Convertible Senior Notes to their principal amount over the term of the Convertible Senior Notes. We will report greater net losses (or lower net income) in our financial results because ASC 470-20 will require interest to include both the current period's amortization of the original issue discount and the instrument's non-convertible interest rate. This could adversely affect our reported or future financial results, the trading price of our common stock and the trading price of the Convertible Senior Notes.

In addition, under certain circumstances, in calculating earnings per share, convertible indebtedness instruments (such as the Convertible Senior Notes) that may be settled entirely or partly in cash may be accounted for utilizing the treasury stock method, the effect of which is that the shares of common stock issuable upon conversion of the Convertible Senior Notes, if any, are not included in the calculation of diluted earnings per share except to the extent that the conversion value of the Convertible Senior Notes exceeds their principal amount. Under the treasury stock method, diluted earnings per share is calculated as if the number of shares of common stock that would be necessary to settle such excess, if we elected to settle such excess in shares, were issued. However, we might not be eligible to use the treasury stock method if, due to cash maintenance requirements under our Term Loan, we can only physically settle conversion of the Convertible Senior Notes. In addition, we cannot be sure that the accounting standards in the future will continue to permit the use of the treasury stock method. If we are unable to use the treasury stock method in accounting for the shares issuable upon conversion of the Convertible Senior Notes, if any, then our diluted earnings per share would be adversely affected. However, if reflecting the Convertible Senior Notes in diluted earnings per share in this manner is anti-dilutive, or if the conversion value of the Convertible Senior Notes does not exceed their principal amount for a reporting period, then the shares underlying the Convertible Senior Notes will not be reflected in our diluted earnings per share.

In August 2020, the FASB issued ASU No. 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40),* or ASU 2020-06, which may change the accounting for the convertible debt instruments described above. Under ASU 2020-06, an entity may no longer be required to separately account for the liability and equity components of convertible debt instruments. This could have the impact of reducing non-cash interest expense, and thereby increasing net income. Additionally, the treasury stock method for calculating earnings per share will no longer be allowed for convertible debt instruments. Rather, the if-converted method will be required. Application of the if-converted method may reduce our reported diluted earnings per share. ASU 2020-06 is effective for public business entities for annual reporting periods, and interim reporting periods within those annual periods, beginning after December 15, 2021 on a prospective basis, and early adoption is permitted. The Company is currently evaluating the impact this guidance will have on its financial statements.

We cannot be sure whether other changes may be made to the current accounting standards related to the Convertible Senior Notes, or otherwise, that could have an adverse impact on our financial statements.

We will continue to incur significant costs as a result of operating as a public company, and our management will continue to devote substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We will continue to incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and regulations regarding corporate governance practices. The listing requirements of The Nasdaq Global Select Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel devote and will need to continue to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations have increased our legal and financial compliance costs and will continue to make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms. Additionally, the recently filed securities and shareholder litigation (see Item 3. Legal Proceedings for description) will require us to incur legal expenses to defend and may result in management time directed towards the litigation.

In addition, we implemented an enterprise resource planning, or ERP, system for our company. An ERP system is intended to combine and streamline the management of our financial, accounting, human resources, sales and marketing and other functions, enabling us to manage operations and track performance more effectively. The ongoing process improvements of our ERP system may result in substantial costs. Additionally, in the future, we may be limited in our ability to convert any business that we acquire to the ERP. Any disruptions or difficulties in using an ERP system could adversely affect our controls and harm our business, including our ability to forecast or make sales and collect our receivables. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention.

Additionally, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404(a) of the Sarbanes-Oxley Act. We are also subject to the compliance requirements of Section 404(b) of the Sarbanes-Oxley Act, which has resulted in us incurring substantial expenses and expending significant management efforts to comply with the Act, which we will continue. We currently have only limited internal audit capabilities and utilize an external firm to provide internal audit services. We will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we are not able to comply with the requirements of Section 404(b) or if we identify or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC, or other regulatory authorities, which would require additional financial and management resources.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize veverimer.

We may seek to establish collaboration or similar agreements with one or more established biotechnology, pharmaceutical or specialty pharmaceutical companies to support the development, regulatory approval and commercialization of veverimer outside of the United States and we may seek similar arrangements for the development or commercialization of veverimer in the United States. We may enter into these arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies for veverimer, both in the United States and internationally. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so choose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations.

Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority.

Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. If we were to enter into any collaboration agreements, any such termination or expiration would adversely affect us financially and could harm our business reputation.

If we engage in acquisitions, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.

Although we currently have no intent to do so, we may attempt to acquire businesses, technologies, services, products or product candidates that we believe are a strategic fit with our business. If we do undertake any acquisitions, the process of integrating an acquired business, technology, service, products or product candidates into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management's attention from our core business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits of any acquisition.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials, including the components of veverimer and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable agencies may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy as well as unexpected changes in tariffs or trade barriers could also strain our suppliers, possibly resulting in supply disruption or increased prices. It may also harm our ability to attract and retain collaboration partners or customers. Additionally, currency fluctuations may affect our ability to successfully market and sell veverimer in markets outside of the United States. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current or future economic climate and financial market conditions could adversely impact our business.

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

Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

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 enterprise financial systems or manufacturing resource planning and enterprise quality systems, 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 currently are limited and are unlikely to prove adequate 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, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain may operate from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

An epidemic or pandemic disease outbreak, including the COVID-19 pandemic, could disrupt our business or operations, including by impacting our ability to recruit and retain an adequate number of trial subjects and protocol compliance by enrolled subjects in VALOR-CKD. Additionally, such an event could also impact the business or operations of our third-party manufacturers and testing laboratories, our CROs, clinical data management organizations, medical institutions and clinical investigators, the FDA or other third parties with whom we conduct business which could have a material adverse effect on our business, results of operations, financial condition and prospects.

An epidemic or pandemic disease outbreak, including the COVID-19 pandemic, could severely disrupt our operations or the operations of third parties that we depend on, including our single third-party contract manufacturers, our CROs, clinical data management organizations, medical institutions and clinical investigators, and the FDA and have a material adverse effect on our business, results of operations, financial condition and prospects. While there is significant uncertainty relating to the potential effect of COVID-19 on our business and operations, infections may become more widespread and travel restrictions may worsen.

Together with our investigators, contract research organizations, or CROs, and other contract service providers, we are regularly assessing the potential impact of the COVID-19 pandemic on recruitment and retention of subjects in, and power of, our ongoing VALOR-CKD trial. At this time, safety monitoring activities, adjudication of endpoint events and provision of clinical trial supplies have not been materially affected by COVID-19. The annualized rate of all-cause mortality in VALOR-CKD is higher than we estimated when designing the trial, in part due to the COVID-19 pandemic. We estimated the study would have an annualized study discontinuation rate, which comprises deaths, subjects lost to follow up and those who withdraw their consent to continue to participate and be followed in the study, of 5%; currently the annualized study discontinuation rate is 6%. While we do not believe the ongoing VALOR-CKD trial has been materially affected to date by the COVID-19 pandemic, to the extent current trends continue, there may be negative impacts on the trial in the future, including but not limited to patient recruitment, retention or powering.

As COVID-19 continues to rapidly spread and even after its spread slows, we may experience various temporary and/or permanent disruptions that could materially adversely affect our business, financial condition, results of operations and prospects, including:

- interruptions or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact approval timelines, including delays or difficulties in FDA trial site visits;
- any impact on our third-party manufacturers or their service, raw material or equipment providers could delay the availability of drug substance or drug product for clinical or commercial use;
- delays and other interruptions in our supply chain of veverimer that may affect our commercial launch and sales of veverimer;
- delays or difficulties in continuing recruitment and/or enrollment of subjects in our ongoing VALOR-CKD trial as a result of COVID-19 outbreaks in regions where the trial is being conducted;
- increased rates of subjects withdrawing from our ongoing VALOR-CKD trial following enrollment as a result of contracting COVID-19, being forced to quarantine or general noncompliance with the clinical trial protocol due to potential exposure to COVID-19;
- delays and other interruptions in our supply chain that may affect our clinical sites' receipt of the supplies and materials needed to conduct our ongoing VALOR-CKD trial;
- delays or difficulties in our initiation of clinical sites, including difficulties in recruiting clinical site investigators and clinical site staff, for our ongoing VALOR-CKD trial;
- changes in local regulations as part of a response to the COVID-19 outbreak which may require us to change the ways in which we conduct our ongoing VALOR-CKD trial which may result in unexpected costs, delays or discontinuance of the trial;
- interruption of key VALOR-CKD clinical trial activities, such as site monitoring, due to limitations on travel imposed or recommended by federal, state or foreign governments, employers and others, or interruption of

clinical trial subject visits and trial procedures, the occurrence of which could affect the integrity of our clinical trial data;

- risk that participants enrolled in our ongoing VALOR-CKD trial acquire COVID-19 while the trial is ongoing, which could impact the results of the trial, including by increasing the number of observed adverse events, including death;
- risk that participants enrolled in our ongoing VALOR-CKD trial who acquire COVID-19 may drop out of the trial or die, which could potentially impair our ability to accrue the required number of primary endpoint events;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of medical facilities serving as trial sites for in our ongoing VALOR-CKD trial and medical staff supporting the conduct of the trial;
- volatility in the price of our common stock causing difficulties in raising funds on acceptable terms or accessing funds from our Term Loan with Hercules; and
- limitations on employee resources that would otherwise be focused on the preparation for our commercial launch and conducting our ongoing VALOR-CKD trial including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home or mass transit disruptions.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could compromise sensitive data and result in material disruptions to our drug development programs or other operational impacts.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants regularly defend against data security incidents, cybersecurity attacks or other IT business continuity risks, and our systems and data are vulnerable to damage from computer viruses, cyber attacks, data loss, ransomware, phishing attacks, industrial espionage, other unauthorized access, technological or human error, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions to our operations and result in material disruptions to our drug development programs. For example, the compromise, corruption, loss or theft of clinical trial data from completed or ongoing clinical trials for our investigational drug candidate could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Certain persons and entities may attempt to penetrate our network, the systems hosting our website or our other networks and systems and may otherwise seek to misappropriate our proprietary or confidential information. Our, or our CROs, contractors, consultants and other third-party service provider's back-up and redundant systems may be insufficient or may fail. To the extent that any disruption or security breach were to result in a compromise, corruption, loss or theft of or other damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and significant costs in remediating the incident, complying with regulatory requirements and defending against claims or regulatory investigations. We may be required to expend significant resources in the response, containment, mitigation of cybersecurity incidents as well as in defense against claims that our information security was unreasonable or otherwise violated applicable laws or contractual obligations. Such events could also adversely affect our competitive position, our reputation could be harmed and the further development of our investigational drug candidate could be delayed.

We are subject to evolving privacy and data protection laws, including the Health Information Portability and Accountability Act, or HIPAA, the EU and UK General Data Protection Regulation (collectively, the "GDPR"), and the California Consumer Protection Act, or CCPA. If we fail to protect personal information or comply with existing or future data protection regulations, our business, financial condition, results of operations and prospects may be materially adversely affected.

Numerous state and federal laws and regulations govern the collection, dissemination, use, privacy, confidentiality, security, availability, integrity, and other processing of personal information. HIPAA establishes a set of national privacy and security standards for the protection of protected health information (as defined in HIPAA), or PHI, by health plans, healthcare clearinghouses and certain healthcare providers, referred to as covered entities, and the business associates with whom such covered entities contract for services. HIPAA requires covered entities and business associates, such as us, to develop and maintain policies with respect to the protection of, use and disclosure of electronic PHI, including the adoption of administrative, physical and technical safeguards to protect such information, and certain notification requirements in the event of a data breach.

By virtue of our clinical trial activities in Europe, we are also subject to European data protection laws, including the GDPR (as implemented in the European Economic Area, or EEA and the United Kingdom, or UK). The GDPR establishes stringent requirements applicable to the processing of personal data (i.e., data which identifies an individual or from which an individual is identifiable), affords various data protection rights to individuals (e.g., the right to erasure of personal data) and imposes potential penalties for serious breaches of up to 4.0% annual worldwide turnover or €20 million, whichever is greater. Individuals (e.g., study subjects) also have a right to compensation for financial or non-financial losses (e.g., distress). There may be circumstances under which a failure to comply with the GDPR, or the exercise of individual rights under the GDPR, would limit our ability to utilize clinical trial data collected on study subjects. The GDPR imposes additional responsibility and liability in relation to our processing of personal data. This may be onerous and materially adversely affect our business, financial condition, results of operations and prospects. The GDPR also prohibits the international transfer of personal data from the EEA/UK to countries outside of the EEA/United Kingdom unless made to a country deemed to have adequate data privacy laws by the European Commission or a data transfer mechanism has been put in place. Until recently, one such data transfer mechanism was the EU-US Privacy Shield, which we are certified to for the facilitation of transfers of non-HR data. However, in July 2020 the Court of Justice of the European Union, or CJEU declared the Privacy Shield to be invalid. The CJEU upheld the validity of standard contractual clauses, or SCCs, as a legal mechanism to transfer personal data but companies relying on SCCs will – need to carry out a transfer privacy impact assessment, which among other things, assesses laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under SCCs will need to be implemented to ensure an essentially equivalent level of data protection to that afforded in the EEA. In turn, the findings of the CJEU will have significant implications for cross-border data flows and may result in compliance costs.

In addition, the interpretation and application of consumer, health-related and data protection laws in the United States, Europe and elsewhere are often uncertain, contradictory and in flux. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. If so, this could result in government-imposed fines or orders requiring that we change our practices, which could adversely affect our business.

In addition, we are subject to various U.S. state laws, including the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020. The CCPA now, among other things, requires covered companies to provide disclosures to California consumers concerning the collection and sale of personal information, and gives such consumers certain qualified privacy rights, including the right to opt-out of certain sales of personal information. Amendments to the CCPA have been made since its enactment, certain provisions of the law will sunset at the end of 2020, and it remains unclear what, if any, further amendments will be made to this legislation or how it will be interpreted. While the CCPA includes certain exemptions for data protected by HIPAA or in certain research contexts, the law covers a wide range of data we may process. The CCPA permits the imposition of civil penalties enforced by the California Attorney General and provides a private right of action for consumers in the event of a breach. Interpretations of the CCPA may continue to evolve with regulatory guidance, and the CCPA will be further amended, through the California Privacy Rights Act that passed by popular referendum in November 2020, and will go into effect in January 2023. Similarly, we are following the development of new data laws in several states around the country, as well as the potential for federal privacy legislation. We cannot yet predict the impact of the CCPA, CPRA or other potential new laws on our business or operations, but it may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain approval required for the commercialization of veverimer.

The research, testing, manufacturing, labeling, approval, selling, import, export, pricing and reimbursement marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory agencies in the United States and other countries, which regulations differ from country to country. Neither we nor any future collaboration partner is permitted to market veverimer in the United States until we receive approval of our NDA from the FDA. We have not obtained marketing approval for veverimer anywhere in the world. Obtaining regulatory approval of our NDA, whether through the Accelerated Approval Program or traditional approval process, can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable

U.S. and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of regulatory approval of products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs, or foreign regulatory equivalents.

Prior to obtaining approval to commercialize a drug candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such drug candidates are safe and effective for their intended uses. The number of nonclinical and clinical studies and trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate.

We were seeking approval for veverimer through the FDA's Accelerated Approval Program, which would allow us to demonstrate an effect on a surrogate endpoint that is reasonably likely to predict veverimer's clinical benefit, but subject to rigorous postmarketing requirements, including the completion of one or more confirmatory postmarketing trials to verify the clinical benefit of veverimer. Thus far, we have been unable to obtain approval of veverimer through the Accelerated Approval Program. In August 2020, we received a CRL from the FDA related to our NDA for veverimer. We held an End-of-Review Type A meeting with the FDA's Division of Cardiology and Nephrology in October 2020. Thereafter, we submitted an FDRR requesting that the OND find that the magnitude of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis associated with CKD and that it can therefore serve as the basis for accelerated approval.

In February 2021, the OND issued a decision on our FDRR. While the OND acknowledged that the TRCA-301 and TRCA-301E trials met their serum bicarbonate endpoints with statistical significance, the OND denied the appeal. In its Appeal Denied Letter, or ADL, the OND not only addressed the issue of magnitude of serum bicarbonate change, but cited all of the deficiencies in the CRL in concluding that the data provided in support of the veverimer NDA did not support approval through the Accelerated Approval Program. The OND concluded that the magnitude of the increases in serum bicarbonate levels shown in the TRCA-301/TRCA-301E trial was not of sufficient size or duration to establish that treatment with veverimer would be reasonably likely to provide a discernible reduction in CKD progression. In addition, the OND found that the intended confirmatory trial, VALOR-CKD (also known as TRCA-303), was underpowered to detect a 13% reduction in slowing of CKD progression. This finding was based on information included in the initial NDA submission, including the placebo-subtracted LS mean change from baseline in serum bicarbonate observed in the TRCA-301/TRCA-301E trial and the original Predictive MA Model. The OND also raised concerns regarding the robustness of the study results given that the veverimer NDA was supported by a single registrational trial (TRCA-301/TRCA-301E), which must, alone, provide persuasive evidence of benefit. Specifically, the OND noted concerns around adequate blinding, the trial results being strongly influenced by a single site, and the majority of sites for the TRCA-301/TRCA-301E trial being in Eastern Europe, where differences in patient management, including concomitant medications and diet, might affect the treatment response to veverimer and raise a concern of the applicability to a U.S. patient population. The OND also stated that, while trial results in the TRCA-301/TRCA-301E trial showed improvement in two patient-reported measures, the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test, the OND viewed this subjective data from a single trial with skepticism in the absence of data from a second trial with similar results, and noted that both endpoints would require rigorous blinding to support robust conclusions. However, the OND noted that both of these changes, if eventually established by one or more additional trials, would indicate a potentially meaningful benefit of veverimer treatment—especially in CKD patients who have physical functional impairments. Separate from the ADL, we previously received feedback from the Division of Clinical Outcome Assessment, or DCOA, that reliance on these physical function endpoints for approval may require further validation.

Based on the ADL, we believe that we now have greater clarity on the potential approval of veverimer through the Accelerated Approval Program. The OND suggested that we meet with the Division to discuss submission of Week 52 serum bicarbonate results from the full randomized trial population of VALOR-CKD and that the trial should include a substantial portion of patients from the United States or from regions with “US-like” patients. If the results of this trial were to demonstrate that veverimer provides a meaningfully larger treatment effect than seen in the TRCA-301/TRCA-301E trial, then this trial, along with the results from the TRCA-301/TRCA-301E trial, could address the concerns raised in the CRL regarding the limitations and the size of the treatment response observed in the TRCA-301/TRCA-301E trial. However, whether the extent of increase in serum bicarbonate in any subsequent submission based on VALOR-CKD would support accelerated approval will remain a review issue, and will, in part, reflect the Division’s assessment of the adequacy (i.e., power) of VALOR-CKD to detect the anticipated treatment effect of CKD progression in a reasonable timeframe.

Although the ADL provides greater clarity on the potential path for approval of veverimer through the Accelerated Approval Program, we believe the timeline to meet the requirements for accelerated approval as suggested in the ADL may not result in the most rapid development path for veverimer. For example, if either of the planned interim analyses in VALOR-CKD for early stopping for efficacy results in positive renal outcomes data, this data could be available before the week 52 serum bicarbonate data from the fully enrolled VALOR-CKD trial suggested in the ADL and could serve as the basis for resubmission of the NDA. We are evaluating several options with respect to the VALOR-CKD trial that are focused on obtaining, prior to the end of 2022, additional data on the effect of veverimer on (1) CKD progression; (2) physical functioning; and (3) serum bicarbonate. We may explore the possibility of stopping the trial early for administrative reasons, which would allow analysis of the data using all alpha remaining at that time. In any event, we believe data from VALOR-CKD will be very important in furthering our understanding of the regulatory path for approval of veverimer. As such, we intend to continue the execution of the VALOR-CKD trial with consideration of both the accelerated and traditional approval pathways. Resubmission of the veverimer NDA may require additional clinical data beyond that provided by the VALOR-CKD trial.

We may decide to pursue a traditional approval process for veverimer rather than accelerated approval. In such case, the FDA could determine that our VALOR-CKD trial as supported by our TRCA-301/TRCA-301E trial may not be sufficient to support approval through the traditional approval process. Results from nonclinical and clinical trials and studies can be interpreted in different ways. Even if we believe the clinical data for our drug candidate is promising, such data may not be sufficient to support approval by the FDA and other regulatory agencies.

Both accelerated and traditional regulatory approval pathways of an NDA or NDA supplement are not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process and we may encounter matters with the FDA that require us to expend additional time and resources and delay or prevent the approval of our investigational drug candidate. For example, the FDA may require us to conduct additional studies or trials for veverimer either prior to approval or postmarketing, such as additional drug-drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects enrolled in our current clinical trials from the United States. Despite the time and expense exerted, failure can occur at any stage. The FDA can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to, the following:

- a drug candidate may not be deemed safe or effective;
- the FDA might not approve our trial design and analysis plan;
- the FDA may not find the data from nonclinical and clinical studies and trials sufficient;
- clinical inspection(s) by the FDA or other regulatory authorities may result in unacceptable findings that could negatively impact approval of veverimer;
- the FDA might not accept or deem acceptable a third-party manufacturers’ processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

If veverimer fails to demonstrate safety and efficacy in clinical trials or does not gain regulatory approval, our business and results of operations will be materially and adversely harmed. Additionally, if the FDA requires that we conduct additional clinical trials, places limitations on veverimer in our label, delays approval to market veverimer or limits the use of veverimer, our business and results of operations may be harmed.

The design of our VALOR-CKD trial may be impacted by clinical data generated while the VALOR-CKD trial is ongoing, including data that may affect key assumptions regarding sample size, endpoints, duration or the underlying standard of care, in which case we may be required to modify our planned clinical trials, or conduct additional clinical trials, or we may decide to stop the trial early for administrative reasons.

If clinical data generated while the VALOR-CKD trial is ongoing, including data that may affect key assumptions regarding sample size, endpoints, duration or the underlying standard of care, impacts the VALOR-CKD trial design, we may be required to modify our planned clinical trials, or conduct additional clinical trials, before we can obtain regulatory approval from the FDA or comparable foreign authorities, and any such modification or additional trial could have a material adverse effect on our expected clinical and regulatory timelines, business, prospects, financial condition and results of operations. We may stop the trial early for administrative reasons, in which case the data may or may not be sufficient to support a resubmission and/or approval of the NDA.

We are conducting and may in the future conduct clinical trials for our investigational drug candidate, veverimer, outside the United States and the FDA may not accept data from such trials.

Although the FDA may accept data from clinical trials conducted outside the United States in support of safety and efficacy claims for veverimer, this is subject to certain conditions. For example, such foreign clinical trials should be conducted in accordance with GCP, including review and approval by an independent ethics committee and obtaining the informed consent from subjects of the clinical trials. The foreign clinical data should also be applicable to the U.S. population and U.S. medical practice, which may be affected by factors such as differences in clinical conditions or study populations.

We conducted the TRCA-101 and TRCA-301/TRCA-301E trials, and are conducting the VALOR-CKD trial with majority enrollment outside the United States and may, in the future, conduct clinical trials of our investigational drug candidates outside the United States. In the TRCA-301 trial, 190 trial subjects were located in Eastern Europe, and 27 trial subjects were located in the U.S. In the TRCA-301E trial, 179 trial subjects were located in Eastern Europe and 17 trial subjects were located in the U.S. The CRL issued by the FDA questions the applicability of the TRCA-301/TRCA-301E trial findings to the U.S. population and practice of medicine. In the VALOR-CKD trial, 74% of the current trial subjects are located in Eastern Europe, and at full enrollment approximately 67% are anticipated to be located in Eastern Europe. In VALOR-CKD, we intend to ensure that no single site in the VALOR-CKD trial provides ≥ 5% of the total number of trial subjects. The FDA may not find such foreign clinical data to be applicable to U.S. patients or the U.S. practice of medicine, due to the potential differences in patient management, including diet and concomitant medications, may have on the treatment effect of veverimer. In such event, we may be required to add additional U.S. subjects to the VALOR-CKD trial. Based on feedback received from the FDA, we have elected to focus future enrollment activities in the VALOR-CKD trial in the United States, Canada and Western Europe, but to meet our goal of completing enrollment in 2021 we may need to enroll subjects in other non-Eastern European countries as well. Despite our focus on geographic areas outside Eastern Europe for future enrollment, the FDA may not be reassured that results of our completed VALOR-CKD trial are relevant to the U.S. population or practice of medicine. In which case, we could be required to conduct one or more additional clinical trials within the United States, which would be costly and time-consuming, and which could have a material and adverse effect on our ability to carry out our business plans.

Even if we receive regulatory approval for veverimer, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, veverimer, 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 veverimer.

Even if a drug is approved by the FDA and/or foreign regulatory agencies, regulatory agencies may still impose significant restrictions on a product's indicated uses or marketing or impose various ongoing requirements. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance. In addition, if a drug receives approval through the FDA's Accelerated Approval Program, it will be subject to special postmarketing requirements, including the completion of postmarketing clinical trials to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw the approval for multiple reasons, including if we fail to conduct any required postmarketing trial with due diligence, a postmarketing trial does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false and misleading.

If veverimer receives approval through the Accelerated Approval Program, it will be subject to ongoing regulatory requirements for conducting postmarketing clinical studies and trials, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, including both federal and state requirements in the United States. In addition, manufacturers, manufacturers' facilities and testing laboratories are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMP. As such, we, our contract manufacturers and testing laboratories are subject to continual review and periodic inspections to assess compliance with cGMP. Furthermore, we, our contract manufacturers and testing laboratories will be required to comply with FDA Pharmacovigilance, or PV, requirements and PV inspections by the FDA. Accordingly, we must conduct the postmarketing trial in a diligent manner and we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for veverimer. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote veverimer for indications or uses for which it does not have FDA approval.

If veverimer receives approval through the Accelerated Approval Program but we fail to conduct the required postmarketing trials with due diligence or such postmarketing trials fail to confirm veverimer's clinical profile or risks and benefits, the FDA may withdraw its approval. If a regulatory agency discovers previously unknown problems with veverimer, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing, or labeling of a product, the regulatory agency may impose restrictions on the product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from veverimer. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Additionally, if we are unable to generate revenue from the sale of veverimer our potential for achieving profitability will be diminished and the capital necessary to fund our operations will be increased.

The regulatory requirements and policies may change, and additional government regulations may be enacted for which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we or any future collaboration partner are not able to maintain regulatory compliance, we or such collaboration partner, as applicable, may face government enforcement action and our business will suffer.

We are seeking regulatory approval to market veverimer for the treatment of metabolic acidosis and slowing of kidney disease progression in patients with metabolic acidosis and CKD, unless we seek

regulatory approval for additional or alternative indications, such as improving physical functioning, we will be prohibited from marketing veverimer for other indications.

We are seeking FDA approval to market veverimer for the treatment of metabolic acidosis and slowing of kidney disease progression in patients with metabolic acidosis associated with CKD, unless we seek regulatory approval for additional or alternative indications, such as improving physical functioning, we cannot be certain what indication and what labeling language will be approved for veverimer, if approved.

The FDA strictly regulates the promotional claims that may be made about prescription products, and veverimer may not be promoted for uses that are not approved by the FDA as reflected in its approved labeling. Under applicable regulations, promoting uses that are not reflected in the FDA-approved labeling, referred to as “off-label” marketing, is prohibited. If we are found to have promoted such off-label uses, we may become subject to significant liability.

We are seeking regulatory approval to market veverimer in the United States. If we want to expand the geographies in which we may market veverimer, we will need to obtain additional regulatory approvals.

We are seeking regulatory approval for veverimer in the United States. In the future, we may attempt to develop and seek regulatory approval to promote and commercialize veverimer outside of the United States. In order to obtain such approvals, we may be required to conduct additional clinical trials or studies to support our applications, which would be time consuming and expensive, and may produce results that do not result in regulatory approvals. Further, we will have to expend substantial time and resources in order to establish the commercial infrastructure or pursue a collaboration arrangement that would be necessary to promote and commercialize veverimer outside of the United States. If we do not obtain regulatory approvals for veverimer in foreign jurisdictions, our ability to expand our business outside the United States will be severely limited.

Our failure to obtain regulatory approvals in foreign jurisdictions for veverimer would prevent us from marketing our products internationally.

The approval procedures vary among countries and can involve additional nonclinical and clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory agencies in other countries. Approval by the FDA does not ensure approval by regulatory agencies in other countries, and approval by one or more foreign regulatory agencies does not ensure approval by regulatory agencies in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. In order to market any product in the European Economic Area, or EEA, and many other foreign jurisdictions, separate regulatory approvals are required. In the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization. Before granting a Marketing Authorization, the competent agencies make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. Similarly, marketing any product in the United Kingdom requires a marketing authorization granted by the MHRA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not be able to file for regulatory approvals or to do so on a timely basis, and, even if we do file, we may not receive necessary approvals to commercialize veverimer in any market. If we do not obtain regulatory approvals for veverimer in foreign jurisdictions, our ability to expand our business outside the United States will be severely limited.

If we fail to comply or are found to have failed to comply with FDA and other laws and regulations related to the promotion of veverimer for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If we receive marketing approval for veverimer, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable laws and regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of veverimer for unapproved uses. We also cannot be sure that our employees or contracted agents will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FFDCA, the federal civil False Claims Act, or FCA, the Prescription Drug Marketing Act, the federal criminal Anti-Kickback Statute, and other alleged violations in connection with the promotion of products for unapproved uses and government reimbursement (e.g. Medicare and/or Medicaid). Many of these investigations originate as "qui tam" actions under the FCA. Under the FCA, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, or other applicable prohibitions we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Individuals can also be subject to imprisonment, and we can be excluded from participating in federal health care programs, such as Medicare and Medicaid, which means our products may not be reimbursed by federal healthcare programs and other entities that participate in federal healthcare programs cannot contract with us. Any such exclusions, fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

If approved, veverimer may cause or contribute to adverse medical events that we are required to report to regulatory agencies and if we fail to do so we could be subject to sanctions that would materially harm our business.

The most commonly reported adverse effects experienced by more patients on veverimer than placebo in the TRCA-101 and TRCA-301/TRCA-301E trials combined were mild to moderate diarrhea and flatulence. If we are successful in commercializing veverimer, FDA and most foreign regulatory agency regulations require that we report certain information about adverse medical events if the product may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of veverimer. If we fail to comply with our reporting obligations, the FDA or a foreign regulatory agency could take action, including criminal prosecution, the imposition of civil monetary penalties, and seizure of our products.

If third-party manufacturers fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.

Before commercial distribution of veverimer, contract manufacturers may be inspected to determine acceptability by the FDA or foreign regulatory agencies for their manufacturing facilities, processes and quality systems, as part of the NDA approval. In addition, pharmaceutical manufacturing facilities are subject to inspection by the FDA and foreign regulatory agencies on a regular basis, before and after product approval. Due to the complexity of the processes used to manufacture pharmaceutical products and product candidates, any potential third-party manufacturer may be unable to continue to pass or initially pass federal, state or international regulatory inspections in a cost-effective manner.

If a third-party manufacturer with whom we contract is unable to comply with manufacturing regulations, veverimer may not be approved, or we may be subject to fines, unanticipated compliance expenses, recall or seizure of our products, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions would adversely affect our financial results and financial condition.

Disruptions at the FDA and other government agencies caused by global health concerns, including the COVID-19 pandemic, could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA's ability to perform routine functions. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials. The FDA has since announced that it is working toward the goal of restarting on-site inspections, but it is currently unclear when or how this will be done. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA and other agencies to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We may be subject to healthcare laws, regulation and enforcement; our failure to comply with these laws or regulations, or our potential involvement in enforcement activities, could have a material adverse effect on our results of operations and financial conditions.

Although we do not currently have any products on the market, we are subject to a variety of regulatory requirements, including healthcare statutory and regulatory requirements and enforcement by the U.S. federal and state governments and the foreign governments of the countries in which we, or our contracted third parties, conduct our business. Even though we are not in a position to make patient referrals and do not bill Medicare, Medicaid, or other government or commercial third-party payers, the federal and state healthcare fraud and abuse laws and regulations may be applicable to our business. The healthcare regulatory laws that affect our current and future operations include, among others:

- the federal Anti-Kickback Statute, which is a criminal law that prohibits, among other things, any person from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward referrals, purchases, orders, or arranging for or recommending the purchase, order, or referral of any item or service for which payment may be made in whole or in part by a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value. The Patient Protection and Affordable Care Act, or PPACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute, so that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and individuals, such as prescribers, patients, purchasers, and formulary managers on the other hand. A conviction for violation of the federal Anti-Kickback Statute results in criminal fines and requires mandatory exclusion from participation in federal health care programs. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute that protect certain common, industry practices from prosecution, the exceptions and safe harbors are drawn narrowly, and arrangements may be subject to scrutiny or penalty if they do not fully satisfy all elements of an available exception or safe harbor. On November 20, 2020, OIG issued two final regulations modifying safe harbors to the federal Anti-Kickback Statute. The first rule, scheduled to take effect January 19, 2021, creates new safe harbors and modifies existing safe harbors to promote certain value-based and coordinated care arrangements and to reduce regulatory burden. The Government Accountability Office found the January 19, 2021 effective date to be premature in light of Congressional Review Act requirements, and this rule is likely subject to the "Regulatory Freeze Pending Review" memorandum issued by the Biden Administration on January 20, 2021, which could further delay implementation. This memorandum freezes implementation of certain regulations and guidance documents issued by the Trump administration that had not yet taken effect as of January 20, 2021 and, for rules that have been issued, recommends opening a new comment period for interested parties. The second rule (the

Rebate Rule) contains two parts. The first part creates a new safe harbor for (i) point-of-sale discounts from pharmaceutical manufacturers to Medicare Part D plans, Medicaid managed care organizations, and their contracted pharmacy benefit managers (PBMs), and (ii) fixed fees for certain services that PBMs provide to pharmaceutical manufacturers. This part of the rule was scheduled to take effect on January 29, 2021, but the Government Accountability Office found the effective date to be premature in light of Congressional Review Act requirements. OIG subsequently delayed the January 29, 2021 effective date to March 22, 2021 in light of pending litigation in the U.S. District Court for the District of Columbia and in accordance with the Biden Administration's regulatory freeze memorandum. The rule's second part excludes from the discount safe harbor price reductions (e.g., rebates) for pharmaceutical products from manufacturers to Part D plans when made directly or indirectly through a PBM, unless the reduction in price is required by law. This change was scheduled to take effect on January 1, 2022, but has been delayed until January 1, 2023 by an order of the District Court in litigation over this rule. Given that implementation of these rules is uncertain, we cannot predict the full impact of these rules and any subsequent related regulatory actions on our future contracts with customers and our future pricing strategies with payers;

- federal civil and criminal false claims laws and civil monetary penalty laws, such as the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam (or "whistleblower") actions, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented claims to the government that are false or fraudulent, or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties of $11,665 to $23,331 per false claim or statement for penalties assessed after June 19, 2020, with respect to violations occurring after November 2, 2015. For example, among other things, pharmaceutical companies have been prosecuted under the FCA in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes (e.g., under the Medicaid Drug Rebate Program), and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payers if they are deemed to "cause" the submission of false or fraudulent claims. Criminal prosecution is also possible for making or presenting a false or fraudulent claim to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, or collectively, HIPAA, which imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon entities subject to the law, such as health plans, healthcare clearinghouses and healthcare providers and their respective business associates that perform services for them that involve individually identifiable health information. HITECH also created tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- under the HIPAA criminal federal healthcare fraud statute, it is a crime to knowingly and willfully execute, or attempt to execute, a scheme or artifice to defraud any health care benefit program or to 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 health care benefit program, in connection with the delivery of or payment for health care benefits, items, or services;

- U.S. and European reporting requirements detailing interactions with and payments to healthcare providers and healthcare organizations, such as the U.S. federal Physician Payments Sunshine Act, or Sunshine Act, which requires, among other things, "applicable manufacturers" of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program to annually report to the Department of Health and Human Services, Centers for Medicare and Medicaid Services, information related to payments and other transfers of value provided to "covered recipients." The term covered recipients includes U.S.-licensed physicians and teaching hospitals, and, for reports submitted on or after January 1, 2022 and covering payments and other transfers of value during calendar year 2021, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. In addition, several U.S. states and localities have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports, and/or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Failure to submit required information may result in civil monetary penalties. Some European countries have adopted laws similar to the Sunshine Act, applicable even in some cases to companies conducting clinical trials but that do not yet have marketing approval;

- state and foreign laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, foreign governments or governmental bodies, or to track and report gifts, compensation and other remuneration provided to physicians and other health care providers, and several recently passed state laws that require disclosures to state agencies and/or commercial purchasers with respect to certain price increases that exceed a certain level as identified in the relevant statutes; and

- state law equivalents of each of the above federal laws, such as the federal Anti-Kickback Statute and FCA which may apply to items or services reimbursed by any third-party payers, including commercial insurers (i.e., so-called "all-payor anti-kickback laws"), as well as state laws that govern the privacy and security of health information or personally identifiable information in certain circumstances, including state health information privacy and data breach notification laws which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus requiring additional compliance efforts.

In addition, the approval and commercialization of veverimer outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. 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.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. The evolving enforcement 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.

Additionally, if our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil, administrative and criminal penalties, damages, and fines; the curtailment or restructuring of our operations; contractual damages; disgorgement; reputational harm; additional oversight and reporting obligations pursuant to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws; exclusion from participation in federal and state healthcare programs; and individual imprisonment, any of which could adversely affect our ability to market veverimer, if approved, and adversely impact our financial results. 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 applicable regulatory agencies or the courts, and their provisions are open to a variety of interpretations.

Legislative or regulatory reforms in the United States may make it more difficult and costly for us to obtain regulatory clearance or approval of veverimer and to produce, market and distribute our products after clearance or approval is obtained.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of veverimer. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;

- changes to manufacturing methods;
- recall, replacement, or discontinuance of veverimer; and
- additional record keeping.

Each of these would likely entail substantial time and cost and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals would harm our business, financial condition and results of operations.

Further, the United States and some foreign jurisdictions have enacted or are considering a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products, if approved, profitably. Among policy makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access.

In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives, including the Patient Protection and Affordable Care Act, or PPACA, which contains provisions that may potentially reduce the profitability of products, including, for example, increased rebates for products sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. There have been ongoing judicial and Congressional challenges to the PPACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the PPACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Although two courts have ruled that this repeal renders the individual mandate unconstitutional, this decision is subject to further appeal. The U.S. Supreme Court granted certiorari in March 2020 and heard oral arguments on November 10, 2020 to consider the lower court rulings and whether the mandate, if ruled unconstitutional, can be severed from the remainder of the PPACA. The case is expected to be decided by mid-2021. Additionally, on December 20, 2019, President Trump signed appropriations legislation for fiscal year 2020 that repealed the so-called "Cadillac" tax on certain high-cost employer-sponsored insurance plans, for tax years beginning after December 31, 2019; the annual fee imposed on certain health insurance providers based on market share, for calendar years beginning after December 31, 2020; and the medical device excise tax on non-exempt medical devices, for sales after December 31, 2019. In the future, there may be additional challenges and amendments to the PPACA. It remains to be seen precisely what new legislation will provide, when it will be enacted, and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare, including the cost of pharmaceutical products.

Additionally, there has been increasing executive, legislative and enforcement interest in the United States with respect to drug pricing practices, at both the federal and state level. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state bills designed to, among other things, lower drug pricing, bring more transparency to drug pricing, review the relationship between pricing and manufacturer sponsored patient support programs, and reform government program reimbursement methodologies for drugs. For example, the Consolidated Appropriations Act, 2021 included several drug price reporting and transparency measures, such as a new requirement for certain Medicare plans to develop tools to display Medicare Part D prescription drug benefit information in real time and for group and health insurance issuers to report information on pharmacy benefit and drug costs to the Secretaries of HHS, Labor, and the Treasury. While any additional proposed measures will require authorization through additional legislation to become effective, Congress has indicated that it will continue to seek new legislative measures to control prescription drug costs.

Changes in the U.S. presidential administration may result in further administrative actions affecting prescription drug pricing, including modifications to administrative measures taken in response to executive orders during the Trump Administration. On July 24, 2020, President Trump signed a series of Executive Orders directing the Secretary of the Department of Health and Human Services to advance certain policies intended to reduce prescription drug prices and out-of-pocket costs for patients, including issuance of final regulations to allow importation of prescription drugs from Canada. The Food and Drug Administration issued a final rule, effective November 30, 2020, permitting the importation of certain prescription drugs from Canada. The Biden administration has expressed support for measures to reduce prescription drug prices, but the future of this rule and its potential impact on our business, is uncertain in light of action by the Canadian government to block bulk exports of prescription drugs if the exports would create a shortage in Canada. On September 13, 2020, President Trump issued another executive order directing the Secretary of the Department of Health and Human Services to pursue implementation of two new payment models under which Medicare would test whether paying no more than the "most-favored-nation" price for certain included drugs and biological products covered under Part B and Part D, respectively, would mitigate poor clinical outcomes and increased Medicare expenditures associated with high drug costs. If implemented, the "most-favored-nation" price would generally reflect the lowest price, after certain adjustments, for a pharmaceutical product sold in an economically-comparable member country of the Organisation for Economic Co-operation and Development. The most-favored nation model was scheduled to begin on January 1, 2021, but implementation has been delayed by litigation, the outcome of which is unclear. Finally, in December 2020, CMS issued a final regulation amending the Medicaid Drug Rebate Program. The rule implements changes to align existing regulations with statutory amendments enacted pursuant to the PPACA, and includes provisions affecting price reporting related to manufacturer-sponsored patient assistance programs subject to PBM accumulator programs, certain value-based purchasing arrangements, line extensions, and authorized generics. Because certain parts of this rule were scheduled to take effect after January 20, 2021, those provisions are subject to the "Regulatory Freeze Pending Review" memorandum issued by the Biden Administration, as discussed above.

At the state level, legislatures and agencies are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including constraints on pricing, discounting and reimbursement; restrictions on certain product access and marketing; cost disclosure and transparency measures that require detailed reporting of drug pricing and marketing information both at product launch and in the event of a price increase; and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. For example, the state of California passed legislation that requires drug manufacturers to notify the state at least 60 days prior to instituting price increases and Maryland passed legislation to create a drug pricing review commission that will evaluate drug cost and recommend setting an upper limit or cap for therapies deemed too expensive. We cannot predict what other reforms may ultimately be implemented at the federal or state level or the effect of any future legislation or regulation and, accordingly, face uncertainties that may result from additional reforms and their impact on our operations. Further, the implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize veverimer and/or those products for which we may receive regulatory approval in the future.

If we fail to obtain and sustain an adequate level of coverage and reimbursement for veverimer by third-party payers, sales would be adversely affected.

While we expect patients who have metabolic acidosis and CKD to need chronic treatment, we anticipate that most patients will rely on coverage and reimbursement by a third-party payer, such as Medicare, Medicaid or a private health insurer, to pay for such treatment. There will be no commercially viable market for veverimer without coverage and reimbursement from third-party payers. Additionally, even if we obtain third-party payer coverage and reimbursement for veverimer, if the level of coverage and reimbursement is below our expectations, or if reimbursement requires stringent prior authorization or other forms of utilization management, our revenue and gross margins will be adversely affected.

Obtaining coverage and reimbursement for a product from a government or other third-party payer can be an expensive and time-consuming process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payer. We cannot be certain if and when we will obtain coverage to allow us to sell veverimer, if approved, into our target markets. Even if we do obtain coverage, third-party payers, periodically review and may question the coverage of, and challenge the prices charged for, our products. Reimbursement rates from third-party payers vary depending on the payer, the insurance plan and other factors. A current trend in the United States health care industry is toward cost containment. Large public and private payers, managed care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payers, including Medicare, are questioning the coverage of, and challenging the prices charged for medical products and services, and many third-party payers limit coverage of, or reimbursement for, newly approved health care products.

In addition, there may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacturing, sales and distribution expenses.

Interim reimbursement levels for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payers, by any future laws limiting drug prices and by any future relaxation of laws that presently restrict imports of product from countries where they may be sold at lower prices than in the United States.

Coverage and reimbursement by a third-party payer may depend upon a number of factors, including the third-party payer's determination that use of a 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.

We cannot be sure that coverage and reimbursement will be available for veverimer and, if coverage and reimbursement are available, what the level of reimbursement will be. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payers for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Reimbursement may impact the demand for, and the price of, veverimer, if approved. Assuming we obtain coverage for veverimer by a third-party payer, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Although we may be able to provide co-pay assistance to some patients with commercial healthcare insurance, some commercial health insurance plans limit how this assistance may count towards a patient's deductible and other cost-sharing requirements. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payers to reimburse all or part of the costs associated with those medications. Patients are unlikely to use veverimer unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of veverimer. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

We expect to experience pricing pressures in connection with the sale of our investigational drug candidate due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and recent legislative proposals. The downward pressure on healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the successful commercialization of new products. Further, the adoption and implementation of any future governmental cost containment or other health reform initiative may result in additional downward pressure on the price that we may receive for veverimer, if approved.

These cost-control initiatives could decrease the price we might establish for veverimer, which could result in product revenue being lower than anticipated. The pricing, coverage and reimbursement of veverimer, if approved, must be adequate to support a commercial infrastructure. If the price for veverimer decreases or if governmental and other third-party payers do not provide adequate coverage and reimbursement levels, our revenue and prospects for profitability will suffer. Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis.

Outside the United States, international operations are generally subject to extensive governmental price controls and market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, China and other countries will put pressure on the pricing and usage of veverimer. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for veverimer, if approved. Accordingly, in markets outside the United States, the reimbursement for veverimer compared with the United States may be insufficient to generate commercially reasonable revenue and profits.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the United States domestic bribery statute contained in 18 U.S.C. § 201, the United States Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell veverimer abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Risks Related to Intellectual Property

We may become subject to claims alleging infringement of third parties' patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of veverimer.

Our success depends in part on our ability to develop, manufacture, market and sell veverimer, if approved, and use our proprietary technologies without alleged or actual infringement, misappropriation or other violation of the patents and other intellectual property rights of third parties. There have been many lawsuits and other proceedings asserting patents and other intellectual property rights in the pharmaceutical and biotechnology industries. We cannot assure you that veverimer will not infringe existing or future third-party patents. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that we may infringe by commercializing veverimer. There may also be issued patents or pending patent applications that we are aware of, but that we think are irrelevant to veverimer, which may ultimately be found to be infringed by the manufacture, sale, or use of veverimer. Moreover, we may face claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. In addition, veverimer has a complex structure that makes it difficult to conduct a thorough search and review of all potentially relevant third-party patents. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of veverimer.

We may be subject to third-party claims in the future against us or our collaborators that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third-party's patents. Furthermore, because of the potential for significant damage awards, which are not necessarily predictable, it is not unusual to find even arguably unmeritorious claims resulting in large settlements. We may be required to indemnify future collaborators against such claims. If a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we or our collaborators may choose to seek, or be required to seek, a license from the third party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we or our collaborators are unable to enter into licenses on acceptable terms. Even if we are successful in defending against such claims, such litigation can be expensive and time consuming to litigate and would divert management's attention from our core business. Moreover, some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. Any of these events could harm our business significantly.

In addition to infringement claims against us, if third parties prepare and file patent applications in the United States that also claim technology similar or identical to ours, we may have to participate in interference or derivation proceedings in the U.S. Patent and Trademark Office, or the USPTO, to determine which party is entitled to a patent on the disputed invention. Recently, due to changes in U.S. law referred to as patent reform, new procedures including *inter partes* review and post-grant review have been implemented. This reform adds uncertainty to the possibility of challenge to our patents in the future. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights with respect to veverimer and our technology. Since patent applications are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our investigational drug candidate.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights or other intellectual property, or those of our licensors. To counter infringement, misappropriation, unauthorized use or other violations, we may be required to file legal claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

We may not be able to prevent, alone or with our licensees or any future licensors, infringement, misappropriation or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from exploiting the claimed subject matter at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from exploiting its technology on the grounds that our patents do not cover such technology. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making, using, importing and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement, misappropriation or other intellectual property litigation, any award of monetary damages we receive may not be commercially valuable. 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 litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

If our intellectual property related to veverimer is not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection, employment and confidentiality agreements to protect the intellectual property related to veverimer. Any disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in foreign countries, and even if issued, the patents may not meaningfully protect veverimer, effectively prevent competitors and third parties from commercializing competitive products or otherwise provide us with any competitive advantage. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Further, the examination process may require us to narrow the claims for our pending patent applications, which may limit the scope of patent protection that may be obtained if these applications issue. Even if patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, patents granted by the European Patent Office may be opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in some jurisdictions third parties can raise questions of validity with a patent office even before a patent has granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. For example, a third party may develop a competitive product that provides therapeutic benefits similar to veverimer but has a sufficiently different composition to fall outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to veverimer is successfully challenged, then our ability to commercialize veverimer could be negatively affected, and we may face unexpected competition that could have a material adverse impact on our business. Further, if we encounter delays in our clinical trials, the period of time during which we could market veverimer under patent protection would be reduced.

Even where laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. If we or one of our future collaborators were to initiate legal proceedings against a third party to enforce a patent covering veverimer, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability against our intellectual property related to veverimer, we would lose at least part, and perhaps all, of the patent protection on veverimer. Such a loss of patent protection would have a material adverse impact on our business. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from exploiting its technology on the grounds that our patents do not cover that technology. Moreover, our competitors could counterclaim that we infringe their intellectual property, and some of our competitors have substantially greater intellectual property portfolios than we do.

We also rely on trade secret protection, employment and confidentiality agreements to protect proprietary know-how that may not be patentable, processes for which patents may be difficult to obtain and/or enforce and any other elements of our product development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees to assign their inventions to us, and endeavor to execute confidentiality agreements with all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology, we cannot be certain that we have executed such agreements with all parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can we be certain that our agreements will not be breached. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. We cannot guarantee that our trade secrets and other confidential proprietary information will not be disclosed or that competitors or third parties such as contract manufacturers will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, we and our third-party suppliers continue to refine and improve the manufacturing process, certain aspects of which are complex and unique, and we may encounter difficulties with new or existing processes. Our reliance on contract manufacturers exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies 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, results of operations and financial condition.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our investigational drug candidate, veverimer.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to veverimer or (ii) invent any of the subject matter claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions to maintain patent applications and issued patents. Noncompliance with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We are in the process of pursuing registered trademarks for a commercial trade name for veverimer in the United States and elsewhere and failure to secure such registrations could adversely affect our business.

We are in the process of pursuing registered trademarks for a commercial trade name for veverimer in the United States and elsewhere. During trademark registration proceedings, our trademark application may be rejected. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties can oppose pending trademark applications and seek to cancel registered trademarks or pursue a claim for trademark infringement. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use with our investigational drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, approval may be delayed or we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. For example, the requirements for patentability may differ in certain countries, particularly developing countries, and we may be unable to obtain issued patents that contain claims that adequately cover or protect veverimer or any future drug candidates. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market veverimer. Consequently, we may not be able to prevent third parties from practicing our technology in all countries outside the United States, or from selling or importing products made using our technology in and into those other jurisdictions where we do not have intellectual property rights. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our investigational drug candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology.

We may be subject to claims that we or our employees, consultants, contractors or advisors have infringed, misappropriated or otherwise violated the intellectual property of a third party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the intellectual property and other proprietary information, know-how or trade secrets of others in their work for us, we may be subject to claims that we or these employees have used or disclosed such intellectual property or other proprietary information. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. To the extent that we fail to obtain such assignments, such assignments do not contain a self-executing assignment of intellectual property rights or such assignments are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

Patent terms may be inadequate to protect our competitive position on our investigational drug candidate, veverimer, for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering veverimer are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of our investigational drug candidate, veverimer, patents protecting veverimer might expire before or shortly after veverimer is commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Intellectual property rights do not necessarily address all potential threats to our business.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. In addition, the degree of future protection afforded by our intellectual property rights is uncertain because even granted intellectual property rights have limitations and may not adequately protect our business. The following examples are illustrative:

- others may be able to make products that are similar to veverimer but that are not covered by the claims of our patent rights;
- the patents of third parties may have an adverse effect on our business;
- we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;

- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we may own or that we exclusively license in the future may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by third parties, including our competitors, public interest groups, or investment firms that engage in short selling activities;
- our competitors might conduct research and development activities in the United States 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 then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our investigational drug candidates or technologies could use the intellectual property of others without obtaining a proper license;
- we may not develop 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 have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Common Stock

Our stock price may be volatile and fluctuate substantially and you may not be able to resell shares of our common stock at or above the price you paid.

The trading price of our common stock has been and is likely to continue to be highly volatile and is subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

- announcement of a CRL from the FDA related to our NDA;
- announcements related to our Type A meeting with the FDA;
- announcements related to our FDRR with the FDA;
- announcements of an ADL from the OND related to our FDRR;
- announcements of regulatory approval of veverimer, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- adverse events experienced by the patient population taking veverimer, whether or not related to our investigational drug candidate;
- changes or developments in laws or regulations applicable to veverimer;
- changes in existing tax laws, treaties or regulations or the interpretations or enforcement thereof, or the enactment or adoption of new tax laws, regulations or policies;
- any adverse changes to our relationship with any manufacturers or suppliers;
- the success of our testing and clinical trials;
- the success of our efforts to scale-up and optimize our manufacturing process;
- the success of our efforts to acquire or license or discover additional drug candidates, if any;
- any intellectual property infringement actions in which we may become involved;

- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the United States equity markets; and
- the loss of any of our key scientific or management personnel.

Following announcement of the deficiency letter from the FDA, there was a significant decline in our stock price. An additional decline occurred after our announcement of the results of the End-of-Review Type A meeting in late October 2020. On January 6, 2021, a putative securities class action was filed in the U.S. District Court for the Northern District of California against Tricida, Inc. and its CEO and CFO (the "Securities Class Action"). Pardi v. Tricida, Inc., et al., 21-cv-00076. The Securities Class Action complaint alleges that during the period September 4, 2019 through October 28, 2020 (the "Class Period"), Tricida and its senior officers violated the federal securities laws, including under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder, through alleged public misrepresentations and/or omissions of material facts concerning Tricida's NDA for veverimer and the likelihood and timing of approval of veverimer by the FDA. No damages amount is specified in the Complaint. Additionally, on February 15, 2021, a derivative action was filed in the District of Delaware, brought by and on behalf of Tricida, Inc. as a Nominal Defendant, against the Company's directors as well as its CEO and CFO (the "Derivative Case"). Ricks v. Alpern et al., Case No, 1:21-cv-000205. The derivative case is based on the allegations of the Securities Class Action and asserts that by allowing the Company and senior executives to make the allegedly false and misleading statements at issue in the Securities Class Action, the defendants breached their fiduciary duties and wasted corporate assets. Additionally, the complaint asserts claims against the senior officers for violation of Sections 10(b) and 21D of the Securities Exchange Act of 1934. No damages amount is specified in the Complaint. The defense of the securities case and the derivative case may cause us to incur substantial costs and may divert the attention of management.

The stock markets in general, and the markets for pharmaceutical and biotechnology stocks in particular, have historically experienced extreme volatility that may have been unrelated to the operating performance of the issuer. Such volatility may continue in the future and may impact our common stock price. The spread of COVID-19, which has caused a broad impact globally, may also materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, it has significantly disrupted global financial markets, and may limit our ability to access capital, which could in the future negatively affect our liquidity. A recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

If securities or industry analysts do not or do not continue to publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business, our stock price and trading volume could decline.

The trading market for our common stock is and will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who currently cover us issue, or in the event we obtain additional coverage and any new analyst issues, an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

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, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. If stockholders who held shares of our common stock prior to our IPO sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

As of December 31, 2020, we had outstanding a total of 50,210,779 shares. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our 2018 Equity Incentive Plan, or 2018 Plan, or our Employee Stock Purchase Plan, or ESPP, will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. The number of shares of our common stock reserved for issuance under the 2018 Plan will automatically increase on the first day of each fiscal year by the lesser of 4% of the number of shares of common stock outstanding on the first day of such fiscal year, 3,200,000 shares of our common stock or such lesser amount as is determined by our board of directors.

The number of shares of our common stock reserved for issuance under the ESPP will automatically increase on the first trading day of each fiscal year by the lesser of 1% of the number of shares of common stock outstanding on the first day of such fiscal year, 800,000 shares of our common stock or such lesser amount as is determined by our board of directors. Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

As of December 31, 2020, all of our outstanding shares of common stock are freely tradable in the public market, other than approximately 18.9 million shares which are subject to trading restrictions. Holders of these shares of our common stock can 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. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2020, our executive officers, directors, holders of 5.0% or more of our capital stock and their respective affiliates beneficially owned approximately 71.6% of our outstanding voting stock.

Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquiror or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with 3-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors, unless the board of directors determines by resolution that any such vacancy shall be filled by the affirmative vote of the stockholders;
- the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of at least 66 2⁄3% of the shares entitled to vote at an election of directors to adopt, amend or repeal certain provisions of our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We are also subject to the anti-takeover provisions contained in Section 203 of the General Corporation Law of the State of Delaware, or the DGCL. Under Section 203 of the DGCL, a corporation may not, in general, engage in a business combination with any holder of 15.0% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Furthermore, certain provisions in the Indenture governing our Convertible Senior Notes may make it more difficult or expensive for a third party to acquire us. For example, the Indenture require us, at the holders' election, to repurchase the Convertible Senior Notes for cash on the occurrence of a fundamental change and, in certain circumstances, to increase the conversion rate for a holder that converts its Convertible Senior Notes in connection with a make-whole fundamental change. A takeover of us may trigger the requirement that we repurchase the Convertible Senior Notes or increase the conversion rate, which could make it more costly for a third party to acquire us. The Indenture also prohibits us from engaging in a merger or acquisition unless, among other things, the surviving entity assumes our obligations under the Convertible Senior Notes and the Indenture. These and other provisions in the Indenture could deter or prevent a third party from acquiring us even when the acquisition may be favorable to holders of the Convertible Senior Notes or our stockholders.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the DGCL, our amended and restated certificate of incorporation, which became effective immediately prior to the completion of our IPO and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.

- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.

- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.

- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.

- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

- We may not retroactively amend our amended and restated certificate of incorporation provisions to reduce our indemnification obligations to directors and officers.

Our amended and restated certificate of incorporation and our amended and restated bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our current or former directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders, any action asserting a claim against us or any of our directors, officers or other employees arising pursuant to the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws, any action asserting a claim against us or any of our directors, officers or other employees that is governed by the internal affairs doctrine, or any other action asserting an "internal corporate claim," as defined in Section 115 of the DGCL. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation and amended and restated bylaws described above. These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our current or former directors, officers or other employees, which may discourage such lawsuits against us and our current or former directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate and our amended and restated bylaws inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be required to pay severance benefits to our executive officers who are terminated in connection with a change in control, which could harm our financial condition or results.

Certain of our executive officers are parties to severance arrangements that contain change in control and severance provisions providing for cash payments for severance and other benefits and acceleration of vesting of stock options in the event of a termination of employment in connection with a change in control of our company. The accelerated vesting of options could result in dilution to our existing stockholders and harm the market price of our common stock. The payment of these severance benefits could harm our financial condition and results. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Additionally, the terms of our Term Loan restrict our ability to pay dividends. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

Our ability to use our net operating losses to reduce our tax liability may be limited.

We have incurred substantial losses during our history. Our ability to utilize net operating loss carryforwards is subject to the rules of Section 382 of the Internal Revenue Code of 1986, as amended, or the Code. Section 382 generally restricts the use of net operating loss carryforwards after an “ownership change.” If we have experienced or experience in the future an “ownership change” for purposes Section 382, we may be subject to annual limits on our ability to utilize net operating loss carryforwards. An ownership change is, as a general matter, triggered by sales or acquisitions of our stock in excess of 50.0% on a cumulative basis during a three-year period by persons or groups of persons owning 5.0% or more of our total equity value. In 2020, the Company performed a Section 382 analysis from inception through June 30, 2020 and concluded that the Company may have experienced multiple ownership changes. The annual limitation may have limited the Company’s ability to utilize net operating losses against taxable income in a given year for both federal and state purposes, however, remaining net operating losses and credit will be available in future years before expiration during their respective carryforward periods. Moreover, we cannot provide any assurance that we will not undergo an ownership change in the future and that our net operating losses will be available. Accordingly, we could pay taxes earlier and/or in larger amounts than would be the case if the net operating losses were available to reduce federal income taxes without restriction.

As noted above under “Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements,” we anticipate that we will continue to incur losses for the foreseeable future. Our ability to utilize any future net operating losses may also be limited by legislation enacted in 2017 commonly referred to as the Tax Cut and Jobs Act, or Tax Act. Under the Tax Act, the amount of post-2017 net operating losses that we are permitted to deduct in any taxable year is limited to 80.0% of our taxable income in such year, where taxable income is determined without regard to the net operating loss deduction itself. In addition, the Tax Act generally eliminates the ability to carry back any net operating loss to prior taxable years, while allowing post-2017 unused net operating losses to be carried forward indefinitely. Recent legislation ameliorates some of these restrictions for losses incurred through 2020, but due to our lack of taxable income we expect our losses to continue to be carried forward past 2020. Due to these changes under the Tax Act, or potential future ownership changes under Section 382 of the Code, we may not be able to realize a tax benefit from the use of our net operating losses, whether or not we attain profitability in future years.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal office is located in South San Francisco, California. On August 14, 2019, we entered into an amendment to the existing operating lease which resulted in a total of 46,074 square feet being leased in aggregate from September 1, 2020. The operating lease ends on August 31, 2027 and we have an option to extend the lease for an additional 36 months subject to certain conditions. We believe that our existing facilities and other available properties will be sufficient to meet our needs for the foreseeable future.

ITEM 3. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties and we may, from time to time, make claims or take legal actions to assert our rights, including intellectual property rights as well as claims relating to employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

On January 6, 2021, a putative securities class action was filed in the U.S. District Court for the Northern District of California against Tricida and its CEO and CFO (the “Securities Class Action”). Pardi v. Tricida, Inc., et al., 21-cv-00076. The Securities Class Action complaint alleges that during the period September 4, 2019 through October 28, 2020 (the “Class Period”), Tricida and its senior officers violated the federal securities laws, including under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder, through alleged public misrepresentations and/or omissions of material facts concerning Tricida’s NDA for veverimer and the likelihood and timing of approval of veverimer by the FDA. The lead plaintiff applications are due on March 7, 2021. No response is currently due to the complaint.

On February 15, 2021 a derivative action was filed in the District of Delaware, brought by and on behalf of Tricida, Inc. as a Nominal Defendant, against the Company’s directors as well as its CEO and CFO (the "Derivative Case"). Ricks v. Alpern et al., Case No, 1:21-cv-000205. The Derivative Case is based on the allegations of the Securities Class Action and asserts that by allowing the Company and senior executives to make the allegedly false and misleading statements at issue in the Securities Class Action, the defendants breached their fiduciary duties and wasted corporate assets. Additionally, the complaint asserts claims against the senior officers for violation of Sections 10(b) and 21D of the Securities Exchange Act of 1934.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Common Stock

Our common stock, $0.001 par value per share, began trading on The Nasdaq Global Select Market on June 28, 2018, under the trading symbol "TCDA".

As of February 19, 2021, there were 399 shareholders of record of our common stock. Certain shares are held in "street" name and, accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number.

Dividends

We have never declared or paid any cash dividends on our common stock. We intend to retain earnings for use in the operation and expansion of our business. Any future determination to pay dividends will be made at the discretion of our board of directors or any authorized committee thereof.

Securities Authorized for Issuance under Equity Compensation Plans

Information regarding the Securities Authorized for Issuance under our Equity Compensation Plans will be included in our definitive Proxy Statement, to be filed relating to our 2020 Annual Meeting of Stockholders and is incorporated herein by reference.

Unregistered Sales of Equity Securities

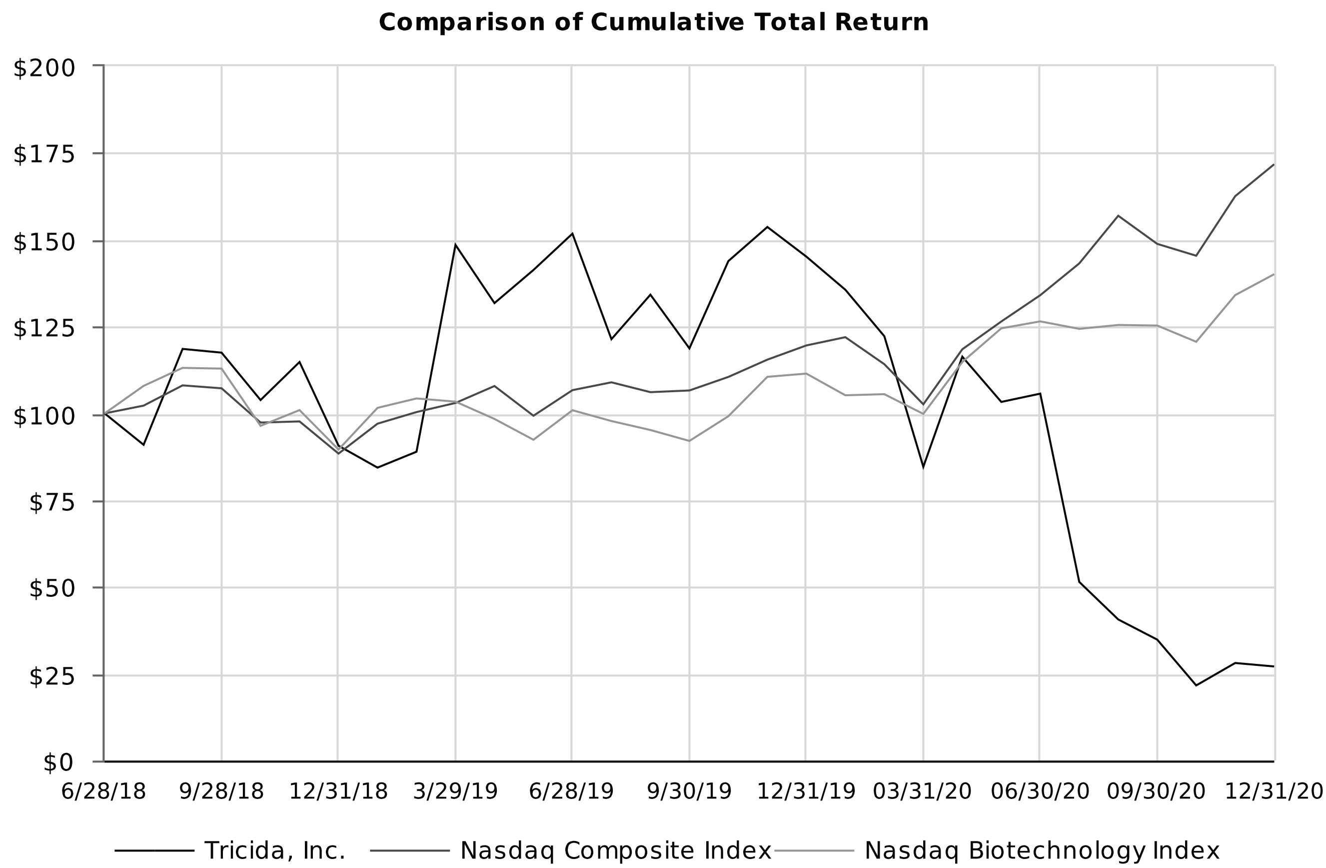
On July 17, 2020, Hercules and Hercules Technology III, L.P. exercised warrants to purchase 85,533 and 21,383 shares, respectively, of the Company's common stock that the Company had issued on February 28, 2018 and December 28, 2018 at an exercise price of $9.35 per share. A total of 68,816 shares of the Company's common stock was issued to Hercules and Hercules Technology III, L.P. in a net settlement transaction. There were no underwriters involved in the transactions and the transactions were exempt from the registration requirements of the Securities Act of 1933, as amended, as a transaction not involving a public offering pursuant to Section 4(a)(2) of that Securities Act of 1933, as amended.

Repurchases of Equity Securities

None.

Stock Performance Graph

The following graph assumes an initial investment of $100 in our common stock on June 28, 2018, the first date that a trade occurred for our stock over-the-counter, as well as the stocks comprising the Nasdaq Composite Index (^IXIC) and the stocks comprising the Nasdaq Biotechnology Index (^NBI). All results assume the reinvestment of dividends, if any. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.



Use of Proceeds from Initial Public Offering of Common Stock

On July 2, 2018, we closed the sale of 13,455,000 shares of common stock, which includes the additional-allotment of 1,755,000 shares exercised by the underwriters in the initial public offering, or IPO, to the public at an IPO price of $19.00 per share. The offer and sale of the shares in the IPO was registered under the Securities Act pursuant to registration statements on Form S-1 (File No. 333-225420), which was filed with the SEC on June 4, 2018 and amended subsequently and declared effective on June 27, 2018, and Form S-1MEF, which was filed with the SEC on June 27, 2018 and became effective on June 27, 2018. The underwriters of the offering were Goldman Sachs & Co. LLC, J.P. Morgan Securities LLC and Cowen and Company, LLC.

We raised approximately $237.7 million in net proceeds after deducting underwriting discounts and commissions of $17.9 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

We invested the funds received in accordance with our investment policy. None of such payments were direct or indirect payments to any of our directors or officers (or their associates), to persons owning ten percent or more of our common stock or to any other affiliates. As described in our final prospectus filed with the SEC on June 29, 2018 pursuant to Rule 424(b) under the Securities Act, we continue to expect to use the net proceeds from our IPO for supporting our activities for our NDA submission and approval process for veverimer (also known as TRC101), manufacturing activities related to veverimer, conducting our safety extension trial, TRCA-301E, and our renal outcomes trial, VALOR-CKD (also known as TRCA-303), commercial expenses related to veverimer, interest payments under our Loan and Security Agreement with Hercules Capital, Inc., and the remainder for working capital and general corporate purposes.

ITEM 6. SELECTED FINANCIAL DATA

The following tables set forth selected financial and other data. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read the financial and other data below in conjunction with Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

	For the Years Ended December 31,				
(in thousands, except share and per share amounts)	2020	2019	2018	2017	2016
Statements of Operations and Comprehensive Loss Data					
Operating expenses:					
Research and development	$ 148,417	$ 133,028	$ 85,594	$ 35,906	$ 21,820
General and administrative	102,983	45,796	18,001	11,216	5,363
Total operating expenses	251,400	178,824	103,595	47,122	27,183
Loss from operations	(251,400)	(178,824)	(103,595)	(47,122)	(27,183)
Change in fair value—preferred stock tranche obligation	—	—	—	5,649	(1,571)
Other income (expense), net	5,016	7,663	3,924	183	103
Interest expense	(18,407)	(5,744)	(3,137)	—	—
Loss before income taxes	(264,791)	(176,905)	(102,808)	(41,290)	(28,651)
Income tax benefit (expense)	—	92	—	—	—
Net loss	(264,791)	(176,813)	(102,808)	(41,290)	(28,651)
Net loss per share, basic and diluted	$ (5.29)	$ (3.72)	$ (4.64)	$ (19.32)	$ (15.69)
Weighted-average number of shares outstanding, basic and diluted	50,027,735	47,521,237	22,146,192	2,137,690	1,826,040

	As of December 31,				
(in thousands)	2020	2019	2018	2017	2016
Balance Sheets Data					
Cash, cash equivalents and investments	$ 332,284	$ 354,978	$ 243,365	$ 67,514	$ 26,450
Working capital	279,757	272,979	229,543	58,202	18,963
Total assets	351,685	371,826	247,849	70,574	27,684
Total liabilities	242,814	107,943	53,324	11,545	8,429
Convertible preferred stock	—	—	—	147,070	66,883
Common stock	50	50	42	2	2
Accumulated deficit	(633,798)	(369,007)	(192,194)	(89,386)	(48,096)
Total stockholders' equity (deficit)	108,871	263,883	194,525	(88,041)	(47,628)

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 financial statements and related notes included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business, include forward-looking statements that involve risks and uncertainties. Investors in our securities should review Item 1A. "Risk Factors" for a discussion of important factors that could cause our 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

Our goal is to slow the progression of chronic kidney disease, or CKD, through the treatment of metabolic acidosis. We are a pharmaceutical company focused on the development and commercialization of our investigational drug candidate, veverimer (also known as TRC101), a non-absorbed, orally-administered polymer designed to treat metabolic acidosis by binding and removing acid from the gastrointestinal tract. Metabolic acidosis is a serious condition commonly caused by CKD and is believed to accelerate the progression of kidney deterioration. It can also lead to bone loss, muscle wasting and impaired physical function. Metabolic acidosis in patients with CKD is typically a chronic disease and, as such, requires long-term treatment to mitigate its deleterious consequences.

There are currently no therapies approved by the U.S. Food and Drug Administration, or FDA, for treating chronic metabolic acidosis. We estimate that metabolic acidosis affects approximately 3 million patients with CKD in the United States, and we believe that treating metabolic acidosis and slowing the progression of CKD in patients with metabolic acidosis and CKD represents a significant unmet medical need and market opportunity.

Veverimer is an in-house discovered, new chemical entity. We have a broad intellectual property estate that we believe will provide patent protection for veverimer until at least 2038 in the United States, at least 2035 in Europe and Russia, and at least 2034 in Australia, China, Hong Kong, Israel, Japan, Mexico and certain other markets.

Veverimer is a low-swelling, spherical polymer bead that is approximately 100 micrometers in diameter. It is a single, high molecular weight, crosslinked polyamine molecule. The size of veverimer prevents systemic absorption from the GI tract. The high degree of cross-linking within veverimer limits swelling and the overall volume in the GI tract, with the goal of facilitating good GI tolerability. The high amine content of veverimer provides proton binding capacity of approximately 10 mEq/gram of polymer. The size exclusion built into the three-dimensional structure of the polymer enables preferential binding of chloride versus larger inorganic and organic anions, including phosphate, citrate, fatty acids and bile acids. This size exclusion mechanism allows a majority of the binding capacity to be used for hydrochloric acid binding.

We submitted our New Drug Application, or NDA, for veverimer through the Accelerated Approval Program as a chronic treatment for metabolic acidosis and slowing of kidney disease progression in patients with metabolic acidosis associated with CKD, for review by the FDA in August 2019. Results from our Phase 3, 12-week efficacy trial, TRCA-301, and a follow-on 40-week extension trial, TRCA-301E, formed the primary basis of our NDA submission. The TRCA-301 trial met both its primary and secondary endpoints in a highly statistically significant manner ($p < 0.0001$ for both the primary and secondary endpoints). The TRCA-301E trial met its primary and all secondary endpoints. The Lancet published the results of the TRCA-301 trial in March 2019 and the results of the TRCA-301E trial in June 2019.

In August 2020, we received a Complete Response Letter, or CRL, from the FDA related to our NDA for veverimer. According to the CRL, the FDA is seeking additional data beyond the TRCA-301/TRCA-301E trial regarding the magnitude and durability of the treatment effect of veverimer on the surrogate marker of serum bicarbonate and expressed concern regarding whether the demonstrated effect size would be reasonably likely to predict clinical benefit. In addition, the CRL questioned the applicability of the treatment effect to the U.S. population and the practice of medicine in the United States. The FDA also expressed concern as to the reliability of the findings given that the findings for the TRCA-301/TRCA-301E trial, were driven by a single, high-enrolling trial site located in Eastern Europe. The CRL did not raise any concerns related to FDA's completed inspection of the highest enrolling clinical trial site in the TRCA-301/TRCA-301E trial and there was no FDA Form 483 issued. There were no safety, clinical pharmacology/biopharmaceutics, CMC, or non-clinical issues identified in the CRL. The CRL provided multiple options for resolving the identified deficiencies, including submission of the data from at least one additional adequate and well-controlled trial demonstrating the efficacy of veverimer for the treatment of metabolic acidosis associated with CKD.

We held an End-of-Review Type A meeting, or Type A meeting, with the FDA's Division of Cardiology and Nephrology, or the Division, in October 2020. The Division agreed, in principle, that an interim analysis of serum bicarbonate data from the VALOR-CKD trial proposed by Tricida could address the Division's concerns regarding the reliability of the TRCA-301/TRCA-301E trial data and the relevance of those trial findings to the U.S. population provided certain conditions were met. Based on other feedback from the FDA during the Type A meeting, we believed the Division would also require evidence of veverimer's effect on CKD progression from a near-term interim analysis of the VALOR-CKD trial for accelerated approval and that the FDA would be unlikely to rely solely on serum bicarbonate data for determination of efficacy. Accordingly, we submitted a Formal Dispute Resolution Request, or FDRR, solely requesting that the Office of New Drugs, or OND, find that the magnitude of serum bicarbonate change seen in the TRCA-301/TRCA-301E trial is reasonably likely to predict clinical benefit in the treatment of metabolic acidosis associated with CKD and that it can therefore serve as the basis for accelerated approval.

In February 2021, the OND issued a decision on our FDRR. While the OND acknowledged that the TRCA-301 and TRCA-301E trials met their serum bicarbonate endpoints with statistical significance, the OND denied the appeal. In its Appeal Denied Letter, or ADL, the OND not only addressed the issue of magnitude of serum bicarbonate change, but cited all of the deficiencies in the CRL in concluding that the data provided in support of the veverimer NDA did not support approval through the Accelerated Approval Program. The OND concluded that the magnitude of the increases in serum bicarbonate levels shown in the TRCA-301/TRCA-301E trial was not of sufficient size or duration to establish that treatment with veverimer would be reasonably likely to provide a discernible reduction in CKD progression. In addition, the OND found that the intended confirmatory trial, VALOR-CKD (also known as TRCA-303), was underpowered to detect a 13% reduction in slowing of CKD progression. This finding was based on information included in the initial NDA submission including the placebo-subtracted LS mean change from baseline in serum bicarbonate observed in the TRCA-301/TRCA-301E trial and the original Predictive MA Model. The OND also raised concerns regarding the robustness of the study results given that the veverimer NDA was supported by a single registrational trial (TRCA-301/TRCA-301E), which must, alone, provide persuasive evidence of benefit. Specifically, the OND noted concerns around adequate blinding, the trial results being strongly influenced by a single site, and the majority of sites for the TRCA-301/TRCA-301E trial being in Eastern Europe, where differences in patient management, including concomitant medications and diet, might affect the treatment response to veverimer and raise a concern of the applicability to a U.S. patient population. The OND also stated that, while trial results in the TRCA-301/TRCA-301E trial showed improvement in two patient-reported measures, the KDQOL Physical Functioning Survey and the Repeated Chair Stand Test, the OND viewed this subjective data from a single trial with skepticism in the absence of data from a second trial with similar results, and noted that both endpoints would require rigorous blinding to support robust conclusions. However, the OND noted that both of these changes, if eventually established by one or more additional trials, would indicate a potentially meaningful benefit of veverimer treatment—especially in CKD patients who have physical functional impairments. Separate from the ADL, we previously received feedback from the Division of Clinical Outcome Assessment, or DCOA, that reliance on these physical function endpoints for approval may require further validation.

Based on the ADL, we believe that we now have greater clarity on the potential approval of veverimer through the Accelerated Approval Program. The OND suggested that we meet with the Division to discuss submission of Week 52 serum bicarbonate results from the full randomized trial population of VALOR-CKD and that the trial should include a substantial portion of patients from the United States or from regions with “U.S.-like” patients. If the results of this trial were to demonstrate that veverimer provides a meaningfully larger treatment effect than seen in the TRCA-301/TRCA-301E trial, then this trial, along with the results from the TRCA-301/TRCA-301E trial, could address the concerns raised in the CRL regarding the limitations and the size of the treatment response observed in the TRCA-301/TRCA-301E trial. However, whether the extent of increase in serum bicarbonate in any subsequent submission based on VALOR-CKD would support accelerated approval will remain a review issue, and will, in part, reflect the Division’s assessment of the adequacy (i.e., power) of VALOR-CKD to detect the anticipated treatment effect of CKD progression in a reasonable timeframe.

Although the ADL provides greater clarity on the potential path for approval of veverimer through the Accelerated Approval Program, we believe the timeline to meet the requirements for accelerated approval as suggested in the ADL may not result in the most rapid development path for veverimer. For example, if either of the planned interim analyses in VALOR-CKD for early stopping for efficacy results in positive renal outcomes data, this data could be available before the week 52 serum bicarbonate data from the fully enrolled VALOR-CKD trial suggested in the ADL and could serve as the basis for resubmission of the NDA. We are evaluating several options with respect to the VALOR-CKD trial that are focused on obtaining, prior to the end of 2022, additional data on the effect of veverimer on (1) CKD progression; (2) physical functioning; and (3) serum bicarbonate. We may explore the possibility of stopping the trial early for administrative reasons, which would allow analysis of the data using all alpha remaining at that time. In any event, we believe data from VALOR-CKD will be very important in furthering our understanding of the regulatory path for approval of veverimer. As such, we intend to continue the execution of the VALOR-CKD trial with consideration of both the accelerated and traditional approval pathways. Resubmission of the veverimer NDA may require additional clinical data beyond that provided by the VALOR-CKD trial.

Our ongoing VALOR-CKD trial is a randomized double-blind, placebo-controlled time-to-event trial. The primary endpoint event in VALOR-CKD is defined as renal death, end-stage renal disease (ESRD) or a confirmed ≥ 40% reduction in estimated glomerular filtration rate (eGFR) (DD40). We anticipate randomizing approximately 1,600 subjects in VALOR-CKD and the trial is currently designed to terminate when the independent blinded Clinical Endpoint Adjudication Committee (CEAC) has positively adjudicated 511 subjects with primary endpoint events, which is anticipated to occur in the first half of 2024. The VALOR-CKD trial also includes interim analyses for early stopping for efficacy after 150 primary endpoint events (anticipated in the second half of 2021, based on the current rate of event accrual) and 250 primary endpoint events (anticipated in mid-2022, based on the current rate of event accrual) have accrued. These interim analyses will be conducted by an independent unblinded Interim Analysis Committee. If the independent unblinded Interim Analysis Committee does not recommend stopping the trial early for efficacy, we will receive no information from these interim analyses. The VALOR-CKD trial also includes, as its first two secondary efficacy endpoints, evaluation of the effect of veverimer versus placebo after one year of treatment on patient-reported and objective measures of physical functioning, using the KDQOL Physical Functioning Survey and the Repeated Chair Stand test, respectively. Although not part of any efficacy endpoints, the VALOR-CKD trial will also provide information regarding the change from baseline in serum bicarbonate in veverimer and placebo-treated subjects.

We initiated enrollment in the VALOR-CKD trial in the fourth quarter of 2018 and have established sites throughout North America, Europe, Latin America and Asia-Pacific. As of February 22, 2021, the VALOR-CKD trial has randomized 1,433 of 1,600 subjects with an average treatment duration of approximately one year and has accrued 69 subjects with positively adjudicated primary endpoint events. In November 2020, based on feedback from the FDA, recruitment for VALOR-CKD was closed in all regions except for the United States, Canada and Western Europe. At the end of recruitment, we anticipate approximately 67% of subjects to be enrolled at Eastern European sites, 19% at U.S., Western European and Canadian sites, 7% at Latin American sites, and 7% at sites in the Asia-Pacific region. Our goal is to complete enrollment by the end of 2021; to meet this goal we may need to reopen recruitment at sites outside of the United States, but we will not reopen recruitment at sites in Eastern Europe. We intend to ensure that no single site in the VALOR-CKD trial provides ≥ 5% of the total number of trial subjects. The FDA's acceptance of the VALOR-CKD data in support of an NDA resubmission, including its assessment of the magnitude and durability of the veverimer treatment effect across the various geographical regions where the study is conducted and the acceptability of the data from non-U.S. countries or regions which will comprise a substantial proportion of the data from the trial, will ultimately be a review issue.

Together with our investigators, contract research organizations, or CROs, and other contract service providers, we are regularly assessing the potential impact of the COVID-19 pandemic on recruitment and retention of subjects in, and power of, our ongoing VALOR-CKD trial. At this time, safety monitoring activities, adjudication of endpoint events and provision of clinical trial supplies have not been materially affected by COVID-19. The annualized rate of all-cause mortality in VALOR-CKD is higher than we estimated when designing the trial, in part due to the COVID-19 pandemic. We estimated the study would have an annualized study discontinuation rate, which comprises deaths, subjects lost to follow up and those who withdraw their consent to continue to participate and be followed in the study, of 5%; currently the annualized study discontinuation rate is 6%. While we do not believe the ongoing VALOR-CKD trial has been materially affected to date by the COVID-19 pandemic, to the extent current trends continue, there may be negative impacts on the trial in the future, including but not limited to patient recruitment, retention or powering. We have provided investigators additional guidance per general FDA and European Medicines Agency, or EMA, recommendations on clinical trial conduct during COVID-19 to ensure the ongoing VALOR-CKD trial is effectively conducted with the utmost attention to trial subject and investigator safety while maintaining compliance with applicable clinical trial regulations and GCP and minimizing risks to the trial's integrity. We will continue to monitor the potential impact that COVID-19 may have on our ongoing VALOR-CKD trial.

At this time, we believe we have sufficient drug substance and access to sufficient drug product manufacturing capacity to supply the anticipated demand of our ongoing VALOR-CKD trial through conclusion of the trial. Veverimer drug substance manufacturing is conducted for us by Patheon Austria GmbH & Co KG, or Patheon, in their Linz, Austria facility. We are in regular communication with Patheon and PCI Pharma Services, our drug product manufacturer and, to our knowledge, there have not been business disruptions at these sites due to COVID-19 affecting the production of veverimer drug substance and drug product. At this time, we have not experienced any material disruption in the distribution network for veverimer, including the provision of raw materials, the shipping of drug substance and drug product and the provision of clinical trial supplies to trial participants.

We have no products approved for marketing, and we have not generated any revenue from product sales or other arrangements. From our inception in 2013 through December 31, 2020, we have primarily funded our operations through the sale of $152.4 million of convertible preferred stock, net proceeds of $237.7 million from our initial public offering, or IPO, on July 2, 2018, net proceeds of $217.9 million from our underwritten public offering on April 8, 2019, net proceeds of $193.3 million from the issuance of Convertible Senior Notes on May 22, 2020 and net borrowing of $72.1 million after fees of $2.9 million under the Loan and Security Agreement, or Term Loan, entered into with Hercules Capital Inc., or Hercules, on February 28, 2018. We have incurred losses in each year since our inception in 2013. Our net losses were $264.8 million, $176.8 million and $102.8 million for the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $633.8 million. Substantially all of our operating losses resulted from expenses incurred in connection with advancing veverimer through development activities and general and administrative costs associated with pre-commercialization activities and administrative functions. At this time, COVID-19 has not materially impacted our current financial resources or our outlook.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect our expenses will continue in connection with our ongoing activities as we:

- conduct clinical studies of veverimer, including the ongoing VALOR-CKD trial;
- continue to optimize the manufacturing processes and manufacture drug substance and drug product to support the ongoing VALOR-CKD trial and the commercial launch, if approved;
- increase our research and development efforts;
- create additional infrastructure to support our product development;
- seek regulatory approval for veverimer, including any activities necessary for the resubmission of the NDA for veverimer;
- maintain, expand and protect our intellectual property portfolio; and
- maintain operational, financial and management information systems to support ongoing operations, including operating as a public company.

We do not expect to generate any revenue from product sales until we successfully complete development and obtain regulatory approval for veverimer. If we obtain regulatory approval for veverimer, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will seek to fund our operations through available cash from our prior equity offerings, the Convertible Senior Note issuance and financing under the Hercules facility, and, as necessary, through additional public or private equity or debt financings or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and ability to develop veverimer.

Components of Our Results of Operations

Research and Development Expense

Research and development expense consists primarily of costs associated with the development of veverimer and includes salaries, bonuses, benefits, travel and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions; expenses incurred under agreements with CROs, investigative sites and consultants that conduct our nonclinical and clinical studies; manufacturing processes optimization and the cost of manufacturing drug substance for commercial and clinical use as well as drug product to support the ongoing VALOR-CKD trial; payments to consultants engaged in the development of veverimer, including stock-based compensation, travel and other expenses; costs related to compliance with quality and regulatory requirements; research and development facility-related expenses, which include direct and allocated expenses, and other related costs. Research and development expense is charged to operations as incurred when these expenditures relate to our research and development efforts and have no alternative future uses. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

All of our research and development expense to date has been incurred in connection with veverimer. We expect our research and development expense to increase for the foreseeable future as we optimize our manufacturing processes and advance veverimer through clinical development, including our ongoing VALOR-CKD trial. The process of conducting clinical studies necessary to obtain regulatory approval is costly and time consuming and the successful development of veverimer is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when, and to what extent, we will generate revenue from commercialization and sale of veverimer, if approved. Therefore, we are unable to estimate with any certainty the costs we will incur in the continued development of veverimer. The degree of success, timelines and cost of development can differ materially from expectations. We may never succeed in achieving regulatory approval for veverimer.

General and Administrative Expense

General and administrative expense consists primarily of salaries, bonuses, benefits, travel, stock-based compensation expense and facility-related expenses for personnel in finance and administrative functions. General and administrative expense also includes professional fees for legal, patent, consulting, accounting and audit services, pre-commercial preparation, medical affairs costs and recruiting services for the potential launch of veverimer and other related costs.

Restructuring Costs

The Company records expenses related to restructuring activities in operating expenses as part of research and development expense and general and administrative expense as appropriate.

On September 10, 2020, the Compensation Committee of the Board of Directors approved the Tricida, Inc. 2020 Reduction in Force Severance Benefit Plan, or 2020 Restructuring Plan. On September 18, 2020, we implemented a restructuring, or Third Quarter 2020 Restructuring, under the 2020 Restructuring Plan to streamline the organization and preserve capital that included the elimination of approximately 21.5% of our workforce as of September 18, 2020 and other cost reductions. Restructuring costs of $2.4 million and $0.3 million were recorded in general and administrative expense and research and development expense, respectively, in our statements of operations and comprehensive loss during the year ended December 31, 2020.

On October 25, 2020, our Board of Directors approved and on October 28, 2020, we implemented a restructuring under the 2020 Restructuring Plan, or Fourth Quarter 2020 Restructuring, to reduce operating costs and better align our workforce with the needs of our business following the completion of the Type A meeting with the FDA in October 2020. The Fourth Quarter 2020 Restructuring resulted in the elimination of approximately 60.0% of our workforce as of October 28, 2020 and included one-time termination severance payments and other employee-related costs, and exit costs including contract termination costs and accelerated depreciation of capitalized software. Restructuring costs of $10.2 million and $0.9 million were recorded in general and administrative expense and research and development expense, respectively, in our statements of operations and comprehensive loss during the year ended December 31, 2020.

Results of Operations

The following table presents our results of operations for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31,			2020 vs. 2019		2019 vs. 2018	
(in thousands)	2020	2019	2018	$	%	$	%
Operating expenses:							
Research and development	$ 148,417	$ 133,028	$ 85,594	$ 15,389	12 %	$ 47,434	55 %
General and administrative	102,983	45,796	18,001	57,187	125 %	27,795	154 %
Total operating expenses	251,400	178,824	103,595	72,576	41 %	75,229	73 %
Loss from operations	(251,400)	(178,824)	(103,595)	(72,576)	41 %	(75,229)	73 %
Other income (expense), net	5,016	7,663	3,924	(2,647)	(35)%	3,739	95 %
Interest expense	(18,407)	(5,744)	(3,137)	(12,663)	220 %	(2,607)	83 %
Loss before income taxes	(264,791)	(176,905)	(102,808)	(87,886)	50 %	(74,097)	72 %
Income tax benefit (expense)	—	92	—	(92)	(100)%	92	N/M
Net loss	$ (264,791)	$(176,813)	$(102,808)	$(87,978)	50 %	$(74,005)	72 %

N/M = Not meaningful

Research and Development Expense

The following table presents our research and development expense for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31,			2020 vs. 2019		2019 vs. 2018	
(in thousands)	2020	2019	2018	$	%	$	%
Clinical development costs	$119,027	$ 99,961	$ 68,483	$ 19,066	19 %	$ 31,478	46 %
Personnel and related costs	15,270	14,840	10,466	430	3 %	4,374	42 %
Stock-based compensation expense	10,966	13,547	2,643	(2,581)	(19)%	10,904	413 %
Other research and development costs	3,154	4,680	4,002	(1,526)	(33)%	678	17 %
Total research and development expense	$148,417	$133,028	$ 85,594	$ 15,389	12 %	$ 47,434	55 %

Research and development expense increased by $15.4 million for the year ended December 31, 2020 compared with the year ended December 31, 2019. The increase was due to activities in connection with our veverimer clinical development program, resulting in increased clinical development costs of $19.1 million related to our manufacturing processes optimization and drug substance manufacturing costs related to our VALOR-CKD trial, partially offset by lower recruiting costs related to the VALOR-CKD trial and our TRCA-301E trial completed in March 2019 and the refund of the veverimer NDA application fee; increased personnel and related costs of $0.4 million related to the Fourth Quarter 2020 Restructuring and the Third Quarter 2020 Restructuring, partially offset by a decrease in bonus expense; a decrease in stock-based compensation expense of $2.6 million related to performance awards granted in 2019 and awards fully vested in 2019, partially offset by annual awards granted in February 2020; and a decrease in other research and development costs of $1.5 million, primarily related to lower travel, recruiting and office expenses.

Research and development expense increased by $47.4 million for the year ended December 31, 2019 compared with the year ended December 31, 2018. The increase was due to activities in connection with our veverimer clinical development program, resulting in increased clinical development costs of $31.5 million related to our VALOR-CKD trial, scale-up costs related to the optimization of our manufacturing process and the veverimer NDA application fee, partially offset by reduced expenditures associated with our TRCA-301 trial completed in May 2018, our drug-drug interaction studies completed in March 2019 and our TRCA-301E trial completed in March 2019; increased personnel and related costs of $4.4 million related to headcount growth; increased stock-based compensation expense of $10.9 million related to headcount growth, performance awards granted in 2019 and higher fair values of awards granted; and increased other research and development costs of $0.7 million, primarily related to facilities and office expenses.

General and Administrative Expense

The following table presents our general and administrative expense for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31,			2020 vs. 2019		2019 vs. 2018	
(in thousands)	2020	2019	2018	$	%	$	%
Personnel and related costs	$ 35,587	$ 12,441	$ 6,760	$ 23,146	186 %	$ 5,681	84 %
Stock-based compensation expense	17,332	11,621	2,509	5,711	49 %	9,112	363 %
Other general and administrative costs	50,064	21,734	8,732	28,330	130 %	13,002	149 %
Total general and administration expense	$102,983	$ 45,796	$ 18,001	$ 57,187	125 %	$ 27,795	154 %

General and administrative expense increased by $57.2 million for the year ended December 31, 2020 compared with the year ended December 31, 2019. The increase was due to pre-commercialization and associated administrative activities in connection with our veverimer clinical development program, resulting in increased personnel and related costs of $23.1 million primarily due to headcount growth in the first half of 2020 and costs related to the Third Quarter 2020 Restructuring and the Fourth Quarter 2020 Restructuring, partially offset by a decrease in bonus expense; increased stock-based compensation expense of $5.7 million due to additional awards in 2020, including annual awards granted in February 2020, partially offset by performance awards granted in 2019; and additional other general and administrative costs of $28.3 million, which primarily related to pre-commercialization activities, medical affairs activities, contract termination costs related to the Third Quarter 2020 Restructuring and the Fourth Quarter 2020 Restructuring, recruiting, training, business insurance premiums and legal services.

General and administrative expense increased by $27.8 million for the year ended December 31, 2019 compared with the year ended December 31, 2018. The increase was due to pre-commercialization and administrative activities in connection with our veverimer clinical development program, resulting in increased personnel and related costs of $5.7 million primarily due to headcount growth; increased stock-based compensation expense of $9.1 million due to headcount growth, performance awards granted in 2019 and higher fair value of awards granted; and additional other general and administrative costs of $13.0 million, which primarily related to pre-commercialization costs, legal services and business insurance premium.

Liquidity and Capital Resources

Sources of Liquidity

From our inception in 2013 through December 31, 2020, we have primarily funded our operations through the sale of $152.4 million of convertible preferred stock, net proceeds of $237.7 million from our IPO on July 2, 2018, net proceeds of $217.9 million from our underwritten public offering on April 8, 2019, net proceeds of $193.3 million from the issuance of Convertible Senior Notes on May 22, 2020 and net borrowing of $72.1 million under the Term Loan. As of December 31, 2020, we had cash, cash equivalents and short-term and long-term investments of $332.3 million.

Hercules Loan and Security Agreement

On February 28, 2018, we entered into the Term Loan with Hercules. The Term Loan provided for a loan in an aggregate principal amount of up to $100.0 million to be funded in five tranches subject to certain performance-based milestones. The first tranche, in the amount of $25.0 million, was funded on the closing date of the Term Loan.

On October 15, 2018, we entered into the second amendment to the Term Loan with Hercules, which amended certain terms of the Term Loan. After giving effect to the second amendment, the Term Loan continued to provide for a loan in an aggregate principal amount of up to $100.0 million to be funded in five tranches subject to certain performance-based milestones. The second tranche was reduced from $25.0 million to $15.0 million and was funded on December 28, 2018.

On March 27, 2019, we modified the Term Loan with Hercules by entering into the third amendment to the Term Loan. After giving effect to the third amendment, the amount available under the Term Loan is increased from up to $100.0 million to up to $200.00 million to be funded in tranches, subject to certain performance-based milestones, and the maturity of the Term Loan is extended. Under the terms of the Term Loan, as amended by the third amendment, the $40.0 million principal outstanding under the Term Loan at the date of the modification remains outstanding, and additional tranches of $20.0 million and $15.0 million will be available for draw down prior to December 15, 2019 and December 15, 2020, respectively. An additional tranche of $75.0 million was to be available for draw down between January 1, 2020 and December 15, 2020, on the condition that we obtain final approval from the FDA of the NDA for veverimer. A final tranche of $50.0 million was to be available for draw down on or prior to December 15, 2021, upon our request and the approval of Hercules' investment committee. On December 13, 2019, the third tranche of the Term Loan was funded in the amount of $20.0 million.

On May 18, 2020, we entered into the fifth amendment to the Term Loan with Hercules. After giving effect to the fifth amendment, the additional tranche of $75.0 million was split into two separate tranches of $25.0 million and $50.0 million. The $25.0 million tranche was to be available for draw down between January 1, 2020 and December 15, 2020, on the condition that we obtained final approval from the FDA of the NDA for veverimer on or before December 15, 2020. The $50.0 million tranche was to be available for draw down between January 1, 2021 and June 30, 2021, on the condition that the $25.0 million tranche had been drawn and final approval had been received for the NDA for veverimer on or before December 15, 2020. A final tranche of $50.0 million was to be available for draw down on or prior to December 15, 2021, upon our request and the approval of Hercules' investment committee. The fifth amendment also permits us to issue certain convertible notes and cash payments to redeem or settle such convertible notes in accordance with the terms thereof. Such cash settlement or redemption is subject to a requirement that we maintain unrestricted cash in an amount not less than 100% of the outstanding obligations under the Term Loan from and after any such cash settlement or redemption, and that there be no default or event of default under the Term Loan at the time of such cash settlement or redemption. On May 19, 2020, the fourth tranche of the Term Loan was funded in the amount of $15.0 million.

The Term Loan bears interest at a floating per annum interest rate equal to the greater of either (i) 8.35% or (ii) the lesser of (x) 8.35% plus the prime rate as reported in The Wall Street Journal minus 6.00% and (y) 9.85%. The maturity date of the Term Loan is April 1, 2023 and we will initially be making interest-only payments until April 1, 2021. Upon expiration of the interest-only period, we will repay the Term Loan in equal monthly installments comprised of principal and interest, based on a 30-month amortization schedule, through maturity. We will pay an additional amount of (a) $2.6 million due on March 1, 2022 and (b) the product of 7.55% and the aggregate loans funded under the Term Loan due at maturity or on any earlier date on which the loans become due. If we prepay the Term Loan, we will be required to pay a prepayment charge equal to (i) 2.00% of the amount being prepaid at any time during the first 12 months following the effective date of the third amendment (ii) 1.50% of the amount being prepaid after 12 months but prior to 24 months following the effective date of the third amendment (iii) 1.00% of the amount being prepaid after 24 months but prior to 36 months following the effective date of the third amendment and (iv) zero if prepaid any time after 36 months following the effective date of the third amendment but prior to the maturity.

On January 6, 2021, we entered into the sixth amendment to the Term Loan with Hercules. The sixth amendment provides for, among other things, a decrease in the amount available under the Term Loan from $200.0 million to $75.0 million. The loan repayment schedule provides for interest only payments until April 1, 2022, followed by consecutive equal monthly amortization payments of principal and interest through the maturity date. The maturity date of the Loan Agreement is October 1, 2023, subject to extension to April 1, 2024 on the condition that we obtain final approval from the FDA for the NDA for veverimer on or before October 1, 2023. The sixth amendment also eliminates prepayment charges for prepayments of principal of the Term Loan made on or after March 1, 2021.

The Term Loan is secured by substantially all of our assets, except our intellectual property, which is the subject of a negative pledge; however, the collateral does consist of rights to payments and proceeds from the sale, licensing or disposition of all or any part of, or rights in, its intellectual property. Under the Term Loan, we are subject to certain covenants, including but not limited to requirements to deliver financial reports at designated times of the year and maintain a minimum level of cash. These covenants also limit or restrict our ability to incur additional indebtedness or liens, acquire, own or make any investments, pay cash dividends, repurchase stock or enter into certain corporate transactions, including mergers and changes of control.

Convertible Senior Notes

On May 22, 2020, we issued $200.0 million aggregate principal amount of 3.50% convertible senior notes due 2027, or Convertible Senior Notes, pursuant to an indenture, dated as of May 22, 2020, or the Indenture, between us and U.S. Bank National Association, as trustee, or the Trustee. The offering and sale of the Convertible Senior Notes were made by us to the initial purchasers in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act of 1933, as amended, or the Securities Act, for resale by the initial purchasers to qualified institutional buyers (as defined in the Securities Act) pursuant to the exemption from registration provided by Rule 144A under the Securities Act. The issuance includes the exercise in full by the initial purchasers of their option to purchase an additional $25.0 million aggregate principal amount of Convertible Senior Notes. Net proceeds from the offering were $193.3 million after deducting underwriting discounts and commissions and other offering costs of approximately $6.7 million.

Our Convertible Senior Notes are senior unsecured obligations, and interest is payable semi-annually in arrears on May 15 and November 15 of each year, beginning on November 15, 2020. The Convertible Senior Notes mature on May 15, 2027, unless earlier repurchased, redeemed or converted and are not redeemable prior to May 20, 2024. We may redeem for cash all or any portion of the Convertible Senior Notes, at our option, on or after May 20, 2024 and on or before the 40th scheduled trading day immediately prior to the maturity date, if the last reported sale price of our common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive), including the trading day immediately preceding the date on which we provide notice of redemption, during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the Convertible Senior Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. We are not required to provide and no sinking fund is provided for the Convertible Senior Notes.

The Convertible Senior Notes are convertible into cash, shares of our common stock or a combination of cash and shares of our common stock at our election at an initial conversion rate of 30.0978 shares of our common stock per $1,000 principal amount of the Convertible Senior Notes, which is equivalent to an initial conversion price of approximately $33.23 per share of our common stock. The conversion rate is subject to customary adjustments for certain events as described in the Indenture. It is our current intent to settle conversions through combination settlement, which involves repayment of the principal portion in cash and any excess of the conversion value over the principal amount in shares of its common stock. As of December 31, 2020, the “if-converted value” did not exceed the remaining principal amount of the Convertible Senior Notes.

Holders may convert their Convertible Senior Notes, at their option, prior to the close of business on the business day immediately preceding February 15, 2027, only under the following circumstances:

- during any fiscal quarter commencing after the calendar quarter ending on September 30, 2020, if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;

- during the five consecutive business day period immediately following any ten consecutive trading day period, or the Measurement Period, in which the trading price per $1,000 principal amount of the Convertible Senior Notes, as determined following a request by a holder of notes in accordance with certain procedures described in the Indenture, for each trading day of the Measurement Period was less than 98% of the product of the last reported sales price of our common stock and the conversion rate on each such trading day;

- upon the occurrence of certain corporate events or distributions of our common stock, as described in the Indenture;

- after our issuance of a notice of redemption; or

- at any time from, and including, February 15, 2027 until the close of business on the trading day immediately before the maturity date.

If we undergo a fundamental change, as described in the Indenture, subject to certain conditions, holders may require us to repurchase for cash all or any portion of their Convertible Senior Notes. The fundamental change repurchase price is equal to 100% of the principal amount of the Convertible Senior Notes to be repurchased, plus accrued and unpaid interest up to, but excluding, the fundamental change repurchase date. In addition, following certain corporate events that occur prior to the maturity date or if we deliver a notice of redemption, we will increase, in certain circumstances, the conversion rate for a holder who elects to convert its Convertible Senior Notes in connection with such a corporate event or notice of redemption, as the case may be.

The Convertible Senior Notes are our senior unsecured obligations and rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the Convertible Senior Notes; equal in right of payment to any of our unsecured indebtedness that is not so subordinated; effectively subordinated in right of payment to any of our secured indebtedness, including secured indebtedness under the Term Loan, to the extent of the value of the assets securing such indebtedness; and structurally subordinated to all indebtedness and other liabilities (including trade payables) of our future subsidiaries, if any.

The Indenture contains customary events of default with respect to the Convertible Senior Notes and provides that upon certain events of default occurring and continuing, the trustee may, and the trustee at the request of holders of at least 25% in principal amount of the Convertible Senior Notes shall declare all principal and accrued and unpaid interest, if any, of the Convertible Senior Notes to be due and payable. In case of certain events of bankruptcy, insolvency or reorganization, involving us or a significant subsidiary, all of the principal of and accrued and unpaid interest on the Convertible Senior Notes will automatically become due and payable.

Funding Requirements

We have incurred losses and negative cash flows from operations since our inception in 2013 and anticipate that we will continue to incur net losses for the foreseeable future. As of December 31, 2020, we had an accumulated deficit of $633.8 million. We expect to incur additional losses in the future to conduct research and development and to conduct pre-commercialization activities and recognize that we may need to raise additional capital to fully implement our business plan.

Such future capital requirements are difficult to forecast and will depend on many factors, including:

- the progress, outcome and results of our ongoing VALOR-CKD trial;
- the costs, timing and success of addressing the deficiencies identified by the FDA in the CRL and issues raised in the ADL related to our NDA for veverimer;
- our ability to obtain approval of our NDA for veverimer from the FDA under either traditional approval or the Accelerated Approval Program, if at all;
- the findings of the FDA during their routine inspections of our facility and the facilities of our contract manufacturers and clinical trial sites during the NDA review process and our ability to promptly and adequately address any such findings;
- the revenue, if any, received from commercial sales of veverimer should we receive regulatory approval;
- our ability to maintain and enforce our intellectual property rights and defend any intellectual property-related claims;
- the costs, timing and success of the scale-up and optimization of the process of manufacturing veverimer, and our minimum and maximum commitments under the Manufacturing and Commercial Supply Agreement we entered into with Patheon on October 4, 2019, as the same may be amended from time to time;
- the costs, timing and success of future commercialization activities, including product manufacturing, marketing, sales and distribution, for veverimer if we receive regulatory approval and do not partner for commercialization;
- the cost of fulfilling our minimum contractual obligations to our suppliers and vendors; and
- the extent to which we acquire or in-license other products and technologies.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic partnerships and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. If we raise additional funds through collaborations, strategic partnerships or licensing arrangements with third parties, we may have to relinquish valuable rights to veverimer, associated intellectual property, our other technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us.

However, there can be no assurance that we will be successful in securing additional funding at levels sufficient to fund our operations or on terms acceptable to us. If we are unsuccessful in our efforts to raise additional financing, we could be required to significantly reduce operating expenses and delay, reduce the scope of or eliminate some of our development programs or our future commercialization efforts, out-license intellectual property rights to our investigational drug candidates and sell unsecured assets, cease operations altogether or a combination of the above, any of which may have a material adverse effect on our business, results of operations, financial condition and/or our ability to fund our scheduled obligations on a timely basis or at all.

On July 2, 2018, we completed our IPO and issued and sold an aggregate of 13,455,000 shares of common stock, including the underwriters' exercise in full of their over-allotment option, a public offering price of $19.00 per share. Net proceeds were approximately $237.7 million, after deducting underwriting discounts and commissions.

On April 8, 2019, we consummated an underwritten public offering and issued 6,440,000 shares of common stock, which included the exercise in full by the underwriters of their option to purchase 840,000 additional shares of common stock at an offering price of $36.00 per share for net proceeds of approximately $217.9 million, after deducting underwriting discounts and commissions of $13.9 million.

On May 22, 2020, we issued $200.0 million aggregate principal amount of 3.50% convertible senior notes due 2027, or Convertible Senior Notes, pursuant to an indenture, dated as of May 22, 2020, or the Indenture, between us and U.S. Bank National Association, as trustee, or the Trustee. The offering and sale of the Convertible Senior Notes were made by us to the initial purchasers in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act of 1933, as amended, or the Securities Act, for resale by the initial purchasers to qualified institutional buyers (as defined in the Securities Act) pursuant to the exemption from registration provided by Rule 144A under the Securities Act. The issuance includes the exercise in full by the initial purchasers of their option to purchase an additional $25.0 million aggregate principal amount of Convertible Senior Notes. Net proceeds from the offering were $193.3 million after deducting underwriting discounts and commissions and other offering costs of approximately $6.7 million.

Cash Flows

The following table summarizes the net cash flow activity for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31,		
(in thousands)	**2020**	**2019**	**2018**
Net cash provided by (used in)			
Operating activities	$ (231,187)	$ (129,590)	$ (94,856)
Investing activities	140,277	(127,498)	(148,354)
Financing activities	210,193	238,490	270,608
Net increase (decrease) in cash and cash equivalents	$ 119,283	$ (18,598)	$ 27,398

Cash Used in Operating Activities

During the year ended December 31, 2020, cash used in operating activities was $231.2 million, which consisted of a net loss of $264.8 million, adjusted by non-cash charges of $38.2 million and changes in our operating assets and liabilities of $4.6 million. The non-cash charges consisted primarily of stock-based compensation of $28.3 million, accretion of Term Loan and Convertible Senior Notes of $8.3 million, depreciation and amortization of $0.9 million, non-cash operating lease costs of $0.8 million and non-cash restructuring costs of $0.7 million partially offset by changes in fair value of compound derivative liability and warrants of $0.8 million. The changes in our operating assets and liabilities were primarily due to a decrease in accrued expenses and other current liabilities of $2.4 million and a decrease in accounts payable of $2.4 million, partially offset by a decrease in prepaid expenses and other assets of $0.2 million.

During the year ended December 31, 2019, cash used in operating activities was $129.6 million, which consisted of a net loss of $176.8 million, adjusted by non-cash charges of $26.1 million and changes in our operating assets and liabilities of $21.1 million. The non-cash charges consisted primarily of stock-based compensation of $25.2 million, amortization of Term Loan discount and issuance costs of $2.2 million, amortization of operating lease right-of-use assets of $1.0 million, changes in fair value of compound derivative liability and warrants of $0.8 million and depreciation and amortization of $0.8 million, partially offset by net amortization of premiums and discounts on investments of $3.7 million. The changes in our operating assets and liabilities were primarily due to an increase in accrued expenses and other current liabilities of $26.0 million, partially offset by a decrease in accounts payable of $2.6 million, an increase in prepaid expenses and other assets of $1.5 million and a decrease in operating lease liabilities of $0.7 million.

During the year ended December 31, 2018, cash used in operating activities was $94.9 million, which consisted of a net loss of $102.8 million, adjusted by non-cash charges of $5.8 million and changes in our operating assets and liabilities of $2.1 million. The non-cash charges consisted primarily of stock-based compensation of $5.2 million, amortization of Term Loan discount and issuance costs of $1.3 million and depreciation and amortization of $0.6 million, partially offset by net amortization of premiums and discounts on investments of $1.1 million. The changes in our operating assets and liabilities were primarily due to an increase in accounts payable of $4.6 million, partially offset by an increase in prepaid expenses and other assets of $1.3 million and a decrease in accrued expenses and other current liabilities of $1.1 million.

Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $140.3 million for the year ended December 31, 2020. Cash used in investing activities was $127.5 million and $148.4 million for the years ended December 31, 2019 and 2018, respectively. The net cash provided by investing activities during the year ended December 31, 2020 was primarily due to proceeds from maturities and paydowns of investments of $429.6 million and proceeds from sale of investments of $41.7 million, partially offset by purchases of investments of $329.4 million and purchases of property and equipment of $1.6 million. The net cash used in investing activities during the year ended December 31, 2019 was primarily due to purchases of investments of $497.5 million and purchases of property and equipment of $1.4 million, partially offset by maturities of investments of $371.4 million. The net cash used in investing activities during the year ended December 31, 2018 was primarily due to purchases of investments of $233.9 and purchases of property and equipment of $0.9 million, partially offset by maturities of investments of $86.4 million.

Cash Provided by Financing Activities

Net cash provided by financing activities was $210.2 million, $238.5 million and $270.6 million for the years ended December 31, 2020, 2019 and 2018, respectively. The net cash provided by financing activities during the year ended December 31, 2020 was primarily due to net proceeds from the issuance of Convertible Senior Notes of $193.3 million, Term Loan funding, net of issuance costs, of $15.0 million and proceeds from the issuance of common stock under equity incentive plans of $2.0 million. The net cash provided by financing activities during the year ended December 31, 2019 was primarily the result of net proceeds from our equity offering of $217.9 million, the Term Loan funding, net of issuance costs, of $18.6 million and proceeds from the issuance of common stock under equity incentive plans of $3.0 million, partially offset by payments of offering costs of $0.9 million. The net cash provided by financing activities during the year ended December 31, 2018 was primarily the result of net proceeds from our IPO of $237.7 million, the Term Loan funding, net of issuance costs, of $38.5 million and proceeds from the issuance of common stock under equity incentive plans of $0.6 million, partially offset by payments of offering costs of $6.6 million.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under the rules of the SEC.

Contractual Obligations

We have contractual obligations from our operating lease, manufacturing and service contracts, Term Loan and tenant improvement loan, and other research and development activities. The following table summarizes our contractual obligations as of December 31, 2020.

(in thousands)	December 31, 2020 Total	2021	2022 - 2023	2024 - 2025	Thereafter
Term Loan(1)	$ 93,067	$ 26,574	$ 66,493	$ —	$ —
Convertible Senior Notes(2)	245,500	7,000	14,000	14,000	210,500
Lease obligations(2)	19,465	2,171	5,780	6,131	5,383
Tenant improvement loan	47	47	—	—	—
Manufacturing and service contracts(3)	566,375	50,961	119,432	121,840	274,142
Total contractual obligations and commitments	$ 924,454	$ 86,753	$ 205,705	$ 141,971	$ 490,025

(1) Comprised of amounts due under the fifth amendment to the Term Loan executed on May 18, 2020. The sixth amendment to the Term Loan executed on January 6, 2021 provides for interest only payments until April 1, 2022.
(2) Comprised of interest payable and principal repayment due under the Convertible Senior Notes' Indenture.
(3) Comprised of the rent payments under the amended lease executed on August 14, 2019.
(4) The purchase obligations are comprised of our non-cancelable purchase commitments under our Manufacturing and Commercial Supply Agreement with Patheon. These amounts are based on forecasts that may include estimates of our future market demand, quantity discounts and manufacturing efficiencies.

We also enter into other contracts in the normal course of business with CROs, contract development and manufacturing organizations and other service providers and vendors. These contracts generally provide for termination on short notice and are cancelable contracts and accordingly, are not included in the contractual obligations and disclosures summarized above.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ significantly from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2. "Summary of Significant Accounting Policies" to our financial statements included in this Annual Report on Form 10-K, we believe that the following accounting policies related to (i) research and development expenses and (ii) stock-based compensation involve significant judgments and estimates used in the preparation of our financial statements.

Research and Development Expenses

Research and development costs are expensed as incurred. Non-refundable advance payments for goods or services that will be used or rendered for future research and development activities are recorded as a prepaid expense and recognized as an expense as the related goods are delivered or the related services are performed.

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing contracts and purchase orders, communicating with internal personnel and external service providers 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 the actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions, contract research organizations that conduct and manage clinical trials on our behalf and contract manufacturing organizations that manage drug production 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 and expense recognition. 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 our estimate, we adjust the accrual accordingly. Furthermore, all additional identified costs incurred are accrued from all outside third-party service providers.

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 our reporting changes in estimates in any particular period. To date, there have been no material differences between our estimates and the amount actually incurred. However, due to the nature of these estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies or other research activity.

Stock-Based Compensation

Stock-based compensation expense represents the grant-date fair value of awards recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis or by using an accelerated attribution method for awards with a performance condition. For stock options and shares purchased under our Employee Stock Purchase Plan, or ESPP, we estimate the grant-date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. For restricted stock units, or RSUs, the grant-date fair value is the closing price of our common stock on the date of grant as reported on The Nasdaq Global Select Market.

The Black-Scholes option-pricing model requires the derivation and use of subjective assumptions to determine the estimated fair value of stock option awards. These assumptions include:

- Expected Term—We have concluded that our stock option exercise history does not provide a reasonable basis upon which to estimate expected term, and therefore we use the simplified method for estimating the expected term of stock option grants. Under this approach, the weighted-average expected term is presumed to be the average of the vesting term and the contractual term of the option.

- Expected Volatility— Beginning in the fourth fiscal quarter of 2019, expected volatility is estimated using a weighted-average historical volatility for our common stock and the historical volatility of the common stock of a representative group of comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. Prior to the fourth fiscal quarter of 2019, since our common stock did not have significant trading history, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty. We will continue to use comparable company information until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants.

- Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the award.

- Dividend Yield—We have not paid dividends on our common stock and do not anticipate paying dividends for the foreseeable future, and we therefore used an expected dividend yield of zero.

In addition to the Black-Scholes assumptions, we include an estimated forfeiture rate in the calculation of stock-based compensation related to stock options and RSUs based on an analysis of our actual forfeitures. We evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors at each reporting period and when we find that actual forfeitures differ materially from our estimates, we record a cumulative adjustment to stock-based compensation expense in that reporting period.

Stock-based compensation expense for stock options with performance conditions is recognized over the estimated service period required to meet performance-based targets using an accelerated attribution method when achieving the performance-based targets is deemed probable. When estimating the service period we make subjective assumptions about the probability and timing of achieving these performance-based targets.

We issue incentive and non-statutory stock options and RSUs under the 2018 Equity Incentive Plan, or 2018 Plan, to certain directors, officers, employees and consultants in consideration for services provided to us. Generally, incentive stock options and non-statutory stock options granted under the 2018 Plan have provided for vesting over a four-year period from either the date of grant or the commencement of service. RSUs granted to directors and vest on the earlier of the one-year anniversary of the award's date of grant, or the date of the Company’s next annual meeting of stockholders that occurs following the date of grant. RSUs granted to certain employees during the year ended December 31, 2020, will vest on December 31, 2021. The 2013 Equity Incentive Plan allows the stock option holders to exercise their stock options prior to vesting. Under the 2018 Plan, exercise of stock options prior to vesting may be allowed on a grant by grant basis. Unvested common stock is issued upon the early exercise of stock options and is subject to repurchase by us at the original exercise price at our option.

Recent Accounting Pronouncements

For details regarding recent accounting pronouncements, see Note 2. "Summary of Significant Accounting Policies" to our financial statements included in this Annual Report on Form 10-K.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

We are exposed to market risk related to changes in interest rates through our available-for-sale investments and we maintain significant amounts of cash at one or more financial institutions that are in excess of federally insured limits.

The primary objective of our investment activities is to preserve capital to fund our operations. Our investments are in commercial paper, U.S. Treasury and government agency securities, commercial paper and corporate debt securities. We consider all highly liquid investments with maturities at the date of purchase of three months or less to be cash equivalents. We classify our investments as available-for-sale in our financial statements. Available-for-sale investments are carried at fair value, with unrealized gains and losses reported as a component of accumulated other comprehensive loss. Realized gains and losses on the sale of all such securities are reported in other income (expense), net and computed using the specific identification method. There were $34 thousand gross realized gains on the sale of available-for-sale investments for the year ended December 31, 2020, and there were no gross realized gains and gross realized losses for the years ended 2019 and 2018. Pursuant to the company's investment policy, all purchased securities have a minimum short-term rating of A1 (Moody's) or P1 (Standard & Poor's) or equivalent. If there is no short-term rating, a purchased security is required to have a long-term rating no lower than A3/A- or equivalent.

Our investments are subject to interest rate risk and could fall in value if market interest rates increase. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our financial statements.

Foreign Exchange Risk

The majority of our transactions occur in U.S. dollars. However, we do have certain transactions with CROs and contract manufacturing organizations that are denominated in currencies other than the U.S. dollar, primarily the Euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against the Euro, or other non-U.S. dollar denominated transactions, affects the reported amounts of expenses, assets and liabilities associated with a limited number of nonclinical and clinical activities. We do not engage in any hedging activity to reduce our potential exposure to currency fluctuations. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our financial statements.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

ITEM 8. FINANCIAL STATEMENTS

TRICIDA, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Tricida, Inc.:

Opinion on the Financial Statements

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

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 26, 2021 expressed an unqualified opinion thereon.

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 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. Our audits included performing procedures to assess the risks 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.

Critical Audit Matter

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Accrued clinical and nonclinical study costs

Description of the Matter	During 2020, the Company incurred $148.4 million for research and development expenses and as of December 31, 2020 accrued $3.8 million for clinical and nonclinical study costs. As described in Note 2 of the Financial Statements, a substantial portion of the Company's ongoing research and development activities are conducted by third-party service providers, including clinical research organizations ("CROs"). External costs to be paid to CROs are accrued and expensed based upon estimates of actual work completed in accordance with signed agreements. The Company estimates the cost of the services not yet invoiced by these service organizations through discussions and other correspondence with internal personnel and the service organizations as to the progress or stage of completion of the services and the agreed-upon fees to be paid for such services. Auditing management's accounting for accrued clinical and nonclinical study costs is especially challenging because the evaluation is dependent upon a high-volume of data and input exchanged between clinical personnel and third-party service providers, such as the number of sites activated, the number of patients enrolled, the number of patient visits, which is tracked in spreadsheets and other end user computing programs. Additionally, due to the long duration of clinical-related development activities and the timing of invoices received from third parties, the determination of the accrual for services incurred requires application of judgment by management. Any delays in the receipt of information related to certain activities in determining the progress to completion of specific tasks conducted for each project can increase the risk of inaccurate assumptions applied to project completion when establishing the cut-off and concluding completeness of costs to be accrued for.
How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's accounting for accrued clinical and nonclinical study expenses, including controls over management's review of clinical trial progress in comparison to budgets and invoices received from third parties, and over the completeness and accuracy of data used in the accrual determination. To test accrued clinical and nonclinical study expenses, our audit procedures included, among others, testing the accuracy and completeness of the underlying inputs used in management's analysis to determine costs incurred. We inspected the terms and conditions of material vendor contracts and change orders, assessed patient visits, pass-through costs, and clinical site costs, and audited the cost models to track progress on service agreements. We evaluated estimated services incurred by third parties by understanding the terms and timeline of significant projects, evaluating management's estimate of work performed and costs incurred, and obtaining external confirmation of key terms and conditions and other key inputs to the accrual calculation, such as the number of patient visits and number of sites activated, for a sample of contracts. Further, we inspected invoices received from third parties after the balance sheet date and performed a lookback analysis to evaluate the completeness of clinical and nonclinical study accruals.

Convertible Debt

Description of the Matter

As described in Note 6 to the financial statements, in May 2020, the Company issued $200.0 million of convertible senior notes due in 2027 (Convertible Notes), which permits the Company to settle in cash, common stock or a combination of cash and common stock at its option.

Auditing the Company's determination of the value allocated to the liability and equity components was complex and judgmental as a result of the significant estimation required to determine the fair value of the liability component, measured at the estimated fair value of similar debt without the conversion option, with the difference between the initial proceeds of the Convertible Notes and the value allocated to the liability component being recognized in stockholders' equity as the carrying amount of the equity component. The fair value of similar debt that does not have an associated conversion option was determined using the Company's effective interest rate. The effective interest rate for the Convertible Notes was estimated using a binomial lattice model with various assumptions, the most significant being expected volatility of the Company's common stock. Additionally, the Company performed a detailed analysis of the terms of the Convertible Notes to identify whether any derivatives that required separate mark-to-market accounting under applicable accounting guidance were present.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls over the Company's initial accounting for, and recording of, the Convertible Notes transaction. For example, we tested the Company's controls over the initial recognition and measurement of the Convertible Notes transaction, including the recording of the associated liability and equity components and the valuation methodology and significant inputs used.

Our testing of the Company's initial accounting for the Convertible Notes transaction, among other procedures, included reading the underlying agreements and evaluating the Company's accounting analysis of the initial accounting of the Convertible Notes transaction, including the determination of the balance sheet classification and identification of any derivatives included in the arrangements.

Our testing of the fair value of the liability component, included, among other procedures, evaluating the Company's selection of the valuation methodology and significant assumptions used by the Company, and evaluating the completeness and accuracy of the underlying data supporting the significant assumptions and estimates. Specifically, when assessing the key assumptions, we evaluated the appropriateness of the Company's estimates of its credit risk, volatility, dividend yield and the market risk free rate as well as its analysis of comparable issuances of debt securities by companies with a similar credit risk rating. In addition, we involved a valuation specialist to assist in our evaluation of the methodology used by the Company and the appropriateness of significant assumptions.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Redwood City, California
February 26, 2021

TRICIDA, INC.

BALANCE SHEETS

(in thousands, except share and per share amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 137,857	$ 18,574
Short-term investments	171,670	289,424
Prepaid expenses and other current assets	4,488	4,744
Total current assets	314,015	312,742
Long-term investments	22,757	46,980
Property and equipment, net	1,112	2,728
Operating lease right-of-use assets	13,801	9,376
Total assets	$ 351,685	$ 371,826
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,508	$ 5,911
Current operating lease liabilities	2,079	1,072
Accrued expenses and other current liabilities	28,671	32,780
Total current liabilities	34,258	39,763
Term Loan, net	76,638	58,374
Convertible Senior Notes, net	118,670	—
Non-current operating lease liabilities	13,046	8,783
Other long-term liabilities	202	1,023
Total liabilities	242,814	107,943
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 40,000,000 shares authorized, no shares issued or outstanding as of December 31, 2020 and December 31, 2019.	—	—
Common stock, $0.001 par value; 400,000,000 shares authorized as of December 31, 2020 and December 31, 2019; 50,210,779 and 49,763,176 shares issued and outstanding as of December 31, 2020 and December 31, 2019, respectively	50	50
Additional paid-in capital	742,555	632,647
Accumulated other comprehensive income (loss)	64	193
Accumulated deficit	(633,798)	(369,007)
Total stockholders' equity	108,871	263,883
Total liabilities and stockholders' equity	$ 351,685	$ 371,826

See accompanying notes to financial statements.

TRICIDA, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2020	2019	2018
Operating expenses:			
Research and development	$ 148,417	$ 133,028	$ 85,594
General and administrative	102,983	45,796	18,001
Total operating expenses	251,400	178,824	103,595
Loss from operations	(251,400)	(178,824)	(103,595)
Other income (expense), net	5,016	7,663	3,924
Interest expense	(18,407)	(5,744)	(3,137)
Loss before income taxes	(264,791)	(176,905)	(102,808)
Income tax benefit (expense)	—	92	—
Net loss	(264,791)	(176,813)	(102,808)
Other comprehensive income (loss):			
Net unrealized gain (loss) on available-for-sale-investments, net of tax	(129)	346	(140)
Total comprehensive loss	$ (264,920)	$ (176,467)	$ (102,948)
Net loss per share, basic and diluted	$ (5.29)	$ (3.72)	$ (4.64)
Weighted-average number of shares outstanding, basic and diluted	50,027,735	47,521,237	22,146,192

See accompanying notes to financial statements.

TRICIDA, INC.

STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY

(in thousands, except share amounts)

	Convertible Preferred Stock		Stockholders' Equity					
			Common Stock					
	Shares	Amount	Shares	Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2017	104,129,702	$ 147,070	2,272,609	$ 2	$ 1,356	$ (13)	$ (89,386)	$ (88,041)
Issuance of Series A convertible preferred stock upon exercise of warrant	95,936	458	—	—	—	—	—	—
Conversion of convertible preferred shares to common stock	(104,225,638)	(147,528)	26,187,321	26	147,502	—	—	147,528
Issuance of common stock in connection with initial public offering, net of underwriter discounts and issuance costs	—	—	13,455,000	13	231,173	—	—	231,186
Reclassification of common stock warrant liability to equity	—	—	—	—	194	—	—	194
Issuance of warrant in connection with Term Loan	—	—	—	—	884	—	—	884
Issuance of common stock under equity incentive plans	—	—	233,317	1	569	—	—	570
Stock-based compensation	—	—	—	—	5,152	—	—	5,152
Net unrealized gain (loss) on available-for-sale investments, net of tax	—	—	—	—	—	(140)	—	(140)
Net loss	—	—	—	—	—	—	(102,808)	(102,808)
Balance at December 31, 2018	—	—	42,148,247	42	386,830	(153)	(192,194)	194,525
Issuance of common stock in connection with public offering, net of underwriter discounts and issuance costs	—	—	6,440,000	6	217,003	—	—	217,009
Issuance of warrants in connection with Term Loan	—	—	—	—	535	—	—	535
Issuance of common stock under equity incentive plans	—	—	1,174,929	2	3,111	—	—	3,113
Stock-based compensation	—	—	—	—	25,168	—	—	25,168
Net unrealized gain (loss) on available-for-sale investments, net of tax	—	—	—	—	—	346	—	346
Net loss	—	—	—	—	—	—	(176,813)	(176,813)
Balance at December 31, 2019	—	—	49,763,176	50	632,647	193	(369,007)	263,883
Equity component of Convertible Senior Notes, net of underwriter discounts and issuance costs	—	—	—	—	79,498	—	—	79,498
Issuance of common stock upon exercise of warrants in connection with Term Loan	—	—	68,816	—	—	—	—	—
Issuance of warrants in connection with Term Loan	—	—	—	—	112	—	—	112
Issuance of common stock under equity incentive plans	—	—	378,787	—	2,000	—	—	2,000
Stock-based compensation	—	—	—	—	28,298	—	—	28,298
Net unrealized gain (loss) on available-for-sale investments, net of tax	—	—	—	—	—	(129)	—	(129)
Net loss	—	—	—	—	—	—	(264,791)	(264,791)
Balance at December 31, 2020	—	$ —	50,210,779	$ 50	$ 742,555	$ 64	$ (633,798)	$ 108,871

See accompanying notes to financial statements.

TRICIDA, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2020	2019	2018
Operating activities:			
Net loss	$ (264,791)	$ (176,813)	$ (102,808)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	897	757	618
Non-cash restructuring costs	679	—	—
Non-cash operating lease costs	845	964	—
Accretion (amortization) of premiums and discounts on investments	1	(3,698)	(1,094)
Accretion of Term Loan and Convertible Senior Notes	8,258	2,173	1,316
Stock-based compensation	28,298	25,168	5,152
Changes in fair value of compound derivative liability and warrants	(775)	816	(188)
Realized gains on sale of investments	(34)	—	—
Other non-cash items	—	(92)	—
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	233	(1,492)	(1,338)
Accounts payable	(2,387)	(2,621)	4,573
Accrued expenses and other liabilities	(2,411)	25,955	(1,087)
Operating lease liabilities	—	(707)	—
Net cash used in operating activities	(231,187)	(129,590)	(94,856)
Investing activities:			
Purchase of investments	(329,441)	(497,492)	(233,928)
Proceeds from maturities of investments	429,606	371,417	86,429
Proceeds from sale of investments	41,717	—	—
Purchase of property and equipment	(1,605)	(1,423)	(855)
Net cash provided by (used in) investing activities	140,277	(127,498)	(148,354)
Financing activities:			
Proceeds from equity offerings, net	—	217,930	237,750
Payments of offering costs	—	(921)	(6,564)
Proceeds from exercise of common stock under equity incentive plans	2,017	3,036	632
Proceeds from issuance of convertible preferred stock, net	—	—	85
Proceeds from Convertible Senior Notes, net	193,285	—	—
Proceeds from leasehold improvement loan	—	—	276
Repayments of leasehold improvement loan	(80)	(106)	(113)
Proceeds from Term Loan, net	14,971	18,551	38,542
Net cash provided by financing activities	210,193	238,490	270,608
Net increase (decrease) in cash and cash equivalents	119,283	(18,598)	27,398
Cash and cash equivalents at beginning of year	18,574	37,172	9,774
Cash and cash equivalents at end of year	$ 137,857	$ 18,574	$ 37,172
Supplemental disclosures			
Cash paid for interest	$ 9,084	$ 3,348	$ 1,612
Supplemental disclosures of non-cash investing and financing activities			
Right-of-use assets obtained in exchange for lease obligations	$ 5,820	$ 8,084	$ —
Warrants and compound derivative liability related to Term Loan	$ 112	$ 535	$ 1,693
Purchases of property and equipment included in accounts payable and accrued expenses	$ —	$ 820	$ 27

See accompanying notes to financial statements.

NOTES TO FINANCIAL STATEMENTS

NOTE 1. ORGANIZATION AND BASIS OF PRESENTATION

Organization—Tricida, Inc., or the Company, was incorporated in the state of Delaware on May 22, 2013 and was granted its certification of qualification in the state of California on August 5, 2013, or inception. The Company is focused on the development and commercialization of its investigational drug candidate, veverimer (also known as TRC101), a non-absorbed, orally-administered polymer designed to treat metabolic acidosis in patients with chronic kidney disease.

The Company has sustained operating losses and expects such annual losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development and commercialization activities for veverimer, for which it expects to incur additional losses in the future. Through December 31, 2020, the Company has relied primarily on the proceeds from equity offerings and debt financing to finance its operations.

The Company recognizes that it may need to raise additional capital to fully implement its business plan, and if market conditions are favorable or if the Company identifies specific strategic opportunities or needs, intends to do so through the issuance of equity, borrowings, or strategic alliances with partner companies. However, if such financing is not available at adequate levels or on reasonable terms, the Company will need to reevaluate its operating plans and could be required to significantly reduce operating expenses and delay, reduce the scope of or eliminate some of its development programs or its future commercialization efforts, out-license intellectual property rights to its investigational drug candidates and sell unsecured assets, or a combination of the above, any of which may have a material adverse effect on its business, results of operations, financial condition and/or its ability to fund its scheduled obligations on a timely basis or at all.

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation— The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States (U.S. GAAP).

Use of Estimates—The preparation of financial statements in conformity with U.S. GAAP requires the Company to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Cash and Cash Equivalents—All highly liquid investments with maturities at the date of purchase of three months or less are classified as cash equivalents. There are no restrictions on cash and cash equivalents.

Investments and Credit Losses—The Company's investments are in U.S. Treasury and government agency securities, commercial paper and corporate debt securities. All investments with maturities of greater than three months at the date of purchase and maturities of less than one year at the reporting date are classified as short-term investments, while investments with maturities of a year or more at the reporting date are classified as long-term investments. The Company has classified its investments as available-for-sale in the accompanying financial statements. Available-for-sale investments are carried at fair value, with unrealized gains and losses reported as a component of accumulated other comprehensive income (loss). Realized gains and losses on the sale of all such securities are reported in other income (expense), net and are computed using the specific identification method.

The Company is exposed to credit losses primarily through its available-for-sale investments. The Company invests excess cash in marketable securities with high credit ratings that are classified in Level 1 and Level 2 of the fair value hierarchy. The Company's investment portfolio at any point in time contains investments in U.S. Treasury and U.S. government agency securities, taxable and tax-exempt municipal notes, corporate notes and bonds, commercial paper, non-U.S. government agency securities and money market funds, and are classified as available-for-sale. The Company assesses whether its available-for sale investments are impaired at each reporting period. Unrealized losses or impairments resulting from the amortized cost basis of any available-for-sale debt security exceeding its fair value are evaluated for identification of credit losses and non-credit related losses. Any credit losses are charged to earnings against the allowance for credit losses of the debt security, limited to the difference between the fair value and the amortized cost basis of the debt security. Any difference between the fair value of the debt security and the amortized cost basis, less the allowance for expected credit losses, are reported in other comprehensive income (loss). Expected cash inflows due to improvements in credit are recognized through a reversal of the allowance for expected credit losses subject to the total allowance previously recognized. The Company's expected loss allowance methodology for the debt securities includes reviewing the extent of the unrealized loss, the size, term, geographical location, and industry of the issuer, the issuers' credit ratings and any changes in those ratings, as well as reviewing current and future economic market conditions and the issuers' current status and financial condition. The Company considered the current and expected future economic and market conditions surrounding the COVID-19 pandemic and determined that the allowance for expected credit losses was not significantly impacted. As of December 31, 2020, the Company has not recognized an allowance for expected credit losses related to available-for-sale investments as the Company has not identified any unrealized losses for these investments attributable to credit factors.

Concentration of Credit Risk and Other Risks and Uncertainties—Financial instruments that potentially subject the Company to a concentration of credit risk, consist primarily of cash, cash equivalents, short-term and long-term investments. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. Management believes that these financial institutions are financially sound, and, accordingly, minimal credit risk exists with respect to those financial institutions. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash, cash equivalents, short-term and long-term investments and by the issuers of the securities to the extent recorded on the balance sheet.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs and prepare for the commercial launch of veverimer. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredient and drug product related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Property and Equipment—Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is determined using the straight-line method over the estimated useful lives of the respective assets, which is three years. Leasehold improvements are amortized using the straight-line method over the shorter of the lease term or their estimated useful economic lives.

Impairment of Long-Lived Assets—Long-lived assets consist of property and equipment. The Company assesses potential impairment losses on long-lived assets used in operations when events and circumstances indicate that assets might be impaired. If such events or changes in circumstances arise, the Company compares the carrying amount of the long-lived assets to the estimated future undiscounted cash flows expected to be generated by the long-lived assets. If the estimated aggregate undiscounted cash flows are less than the carrying amount of the long-lived assets, an impairment charge, calculated as the amount by which the carrying amount of the assets exceeds the fair value of the assets, is recorded. The fair value of the long-lived assets is determined based on the estimated discounted cash flows expected to be generated from the long-lived assets. The Company has recognized an impairment loss of $0.7 million for the year ended December 31, 2020. See Note 10. "Restructuring" for additional details. There were no impairment losses recognized for the years ended December 31, 2019 and 2018.

Deferred Offering Costs—The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in the statements of convertible preferred stock and stockholders' equity as a reduction of additional paid-in capital generated as a result of the equity financing.

Clinical and Manufacturing Accruals—The Company records accruals for the estimated costs of research, nonclinical and clinical studies and manufacturing development, which are a significant component of research and development expenses. A substantial portion of the Company's ongoing research and development activities is conducted by third-party service providers, including clinical research organizations, or CROs, and contract manufacturing organizations, or CMOs. The Company's contracts with CROs generally include pass-through fees such as regulatory expenses, investigator fees, travel costs and other miscellaneous costs, including shipping and printing fees. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts. The Company accrues the costs incurred under agreements with these third parties based on estimates of actual work completed in accordance with the respective agreements. The Company determines the estimated costs through the review of contracts and subsequent discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fees to be paid for such services.

The Company makes significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, the Company adjusts its accruals. Although the Company does not expect its estimates to be materially different from amounts actually incurred, the Company's understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in the Company reporting amounts that are too high or too low in any particular period. The Company's accrual is dependent, in part, upon the receipt of timely and accurate reporting from information provided as part of its clinical and nonclinical studies and other third-party vendors. For the three years ended December 31, 2020, 2019, and 2018, there have been no material differences from the Company's accrued estimated expenses to the actual clinical trial and manufacturing expenses. However, variations in the assumptions used to estimate accruals, including, but not limited to the number of patients enrolled, the rate of patient enrollment, the actual services performed, and the amount of manufactured drug substance and/or drug product, and related costs may vary from the Company's estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect its financial position and results of operations.

Leases—The Company determines if an arrangement contains a lease at inception. For arrangements where the Company is the lessee, operating leases are included in operating lease right-of-use, or ROU, assets; current operating lease liabilities; and non-current operating lease liabilities on its balance sheets. The Company currently does not have any finance leases.

Operating lease ROU assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. ROU assets also include any initial direct costs incurred and any lease payments made on or before the lease commencement date, less lease incentives received. The Company uses its incremental borrowing rate based on the information available at the commencement date in determining the lease liabilities as the Company's leases generally do not provide an implicit rate. The incremental borrowing rate is reevaluated upon a lease modification. The operating lease ROU asset also includes any initial direct costs and prepaid lease payments made less any lease incentives. The Company considered information available at the adoption date of Accounting Standards Update, or ASU, No. 2016-02, *Leases (Topic 842)*, or Topic 842, to determine the incremental borrowing rate for leases in existence as of this date. Lease terms may include options to extend or terminate the lease when the Company is reasonably certain that the option will be exercised. Lease expense is recognized on a straight-line basis over the lease term.

The Company elected to apply each of the practical expedients described in Topic 842 which allow companies not to reassess: (i) whether any expired or existing agreements contain leases, (ii) the classification of any expired or existing leases, and (iii) the capitalization of initial direct costs for any existing leases. In addition, the Company elected not to separate lease and non-lease components of a lease, and to apply the short-term lease measurement and recognition exemption in which ROU assets and lease liabilities are not recognized for short-term operating leases. A short-term lease is a lease that, at the commencement date, has a lease term of 12 months or less and does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise.

Term Loan—The Company accounts for the Loan and Security Agreement, or Term Loan, with Hercules Capital, Inc., or Hercules, as a liability measured at net proceeds less debt discount and is accreted to the face value of the Term Loan over its expected term using the effective interest method. The Company considers whether there are any embedded features in its debt instruments that require bifurcation and separate accounting as derivative financial instruments pursuant to Accounting Standards Codification, or ASC, Topic 815, *Derivatives and Hedging*.

Convertible Senior Notes—At issuance, the Convertible Senior Notes were bifurcated into liability and equity components and accounted for separately. The carrying amount of the debt component was calculated based on the fair value of similar debt instruments that do not have an associated convertible feature. The debt component was recorded as a liability, net of underwriter discounts and issuance costs, and is accreted to face value over the expected term using the effective interest method. The carrying amount of the equity component, representing the conversion option, was determined by deducting the fair value of the liability component from the par value of the Convertible Senior Notes and was recorded, net of allocated underwriter discounts and issuance costs, in additional paid-in capital. The equity component is not remeasured as long as it continues to meet the conditions of equity classification.

Convertible Preferred Stock—The Company recorded all shares of convertible preferred stock at their respective fair values, net of issuance costs, on the dates of issuance. Upon the closing of the Initial Public Offering, or IPO, on July 2, 2018, the 104,225,638 shares of convertible preferred stock outstanding were automatically converted into 26,187,321 shares of common stock.

Warrants—The Company issued freestanding warrants to purchase shares of common stock in connection with its Term Loan. The warrants are recorded at fair value using the Black-Scholes option pricing model. See Note 6 "Borrowings" for additional details.

Research and Development Expense—Research and development expense is charged to the statements of operations and comprehensive loss in the period in which they are incurred. Research and development expense consists primarily of salaries and related costs, including stock-based compensation expense, for personnel and consultants in our research and development functions; fees paid to clinical consultants, clinical trial sites and vendors, including CROs, costs related to pre-commercialization manufacturing activities including payments to CMOs and other vendors and consultants, costs related to regulatory activities, expenses related to lab supplies and services and depreciation and other allocated facility-related and overhead expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Stock-Based Compensation—Stock-based compensation expense represents the grant-date fair value of awards recognized on a straight-line basis or by using an accelerated attribution method for awards with performance conditions over the employee's requisite service period (generally the vesting period). The Black-Scholes option-pricing model is used to calculate the grant date fair value of stock option awards and shares purchased under the Employee Stock Purchase Plan, or ESPP. For restricted stock units, or RSUs, the grant-date fair value is the closing price of the Company's common stock on the date of grant as reported on The Nasdaq Global Select Market. Because stock compensation expense is an estimate of awards ultimately expected to vest, it is reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates. Compensation expense for performance-based awards is recorded over the estimated service period using an accelerated attribution method when the performance conditions are deemed probable of achievement.

The Company records the expense attributed to nonemployee services paid with stock option awards based on the estimated fair value of the awards determined using the Black-Scholes option pricing model. The measurement of stock-based compensation for nonemployees was previously subject to remeasurement as the options vested. As of July 1, 2018, the Company adopted ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which no longer subjects nonemployee awards to remeasurement. The expense is recognized over the period during which services are received.

Restructuring costs—The Company records estimated expense for restructuring activities when such costs are deemed probable and estimable, when approved by the appropriate corporate authority and by accumulating detailed estimates of costs for such plans. These expenses include the estimated costs of employee severance and related benefits, impairment or accelerated depreciation of capitalized software and any other qualifying exit costs such as contract termination costs. These estimates are evaluated periodically to determine whether an adjustment is required.

Income Taxes—The Company accounts for income taxes using the liability method, whereby deferred tax asset and liability account balances are determined based on differences between the financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company provides a valuation allowance when it is more likely than not that some portion or all of its deferred tax assets will not be realized.

The Company accounts for income tax contingencies using a benefit recognition model. If it considers that a tax position is more likely than not to be sustained upon audit, based solely on the technical merits of the position, it recognizes the benefit. The Company measures the benefit by determining the amount that is greater than 50% likely of being realized upon settlement, presuming that the tax position is examined by the appropriate taxing authority that has full knowledge of all relevant information. The Company’s policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Comprehensive Loss—Comprehensive loss is comprised of net loss and other comprehensive income (loss). Other comprehensive income (loss) includes changes in stockholders' equity that are excluded from net loss, primarily unrealized gains or losses on the Company's available-for-sale investments. These changes in stockholders' equity are reflected net of tax.

Net Loss per Share—Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

Segment Reporting—The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. All of the Company's assets are maintained in the United States.

Recent Accounting Pronouncements

Adopted Standards

Effective January 1, 2020, the Company adopted ASU No. 2016-13, F*inancial Instruments—Credit Losses (Topic 326)*, or ASU 2016-13, which changed the impairment model for most financial assets and certain other instruments. The Company adopted ASU 2016-13 on January 1, 2020, using a modified retrospective transition method, which requires a cumulative-effect adjustment, if any, to the opening balance of retained earnings to be recognized on the date of adoption with prior periods not restated. The adoption of ASU 2016-13 did not have a significant impact on the Company's financial statements. See "Credit Losses" above for a description of the Company's credit losses accounting policy.

Standards Not Yet Effective

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, or ASU 2019-12, which simplifies the accounting for income taxes. ASU 2019-12 is effective for public business entities for annual reporting periods, and interim periods within those annual periods, beginning after December 15, 2020 on a prospective basis, and early adoption is permitted. The Company does not expect the adoption of ASU 2019-12 will have a significant impact on its financial statements.

In August 2020, the FASB issued ASU No. 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40),* or ASU 2020-06. ASU 2020-06 simplifies the accounting for convertible debt instruments and convertible preferred stock by removing the existing guidance in *Accounting Standards Codification, or ASC, 470-20, Debt – Debt with Conversion and Other Options*, or ASC 470-20, that requires entities to account for beneficial conversion features and cash conversion features in equity, separately from the host convertible debt or preferred stock. The guidance in ASC 470-20 applies to convertible instruments for which the embedded conversion features are not required to be bifurcated from the host contract and accounted for as derivatives. In addition, the amendments revise the scope exception from derivative accounting in *ASC 815-40, Derivatives and Hedging – Contracts in Entity's Own Equity,* for freestanding financial instruments and embedded features that are both indexed to the issuer's own stock and classified in stockholders' equity, by removing certain criteria required for equity classification. These amendments are expected to result in more freestanding financial instruments qualifying for equity classification (and, therefore, not accounted for as derivatives), as well as fewer embedded features requiring separate accounting from the host contract. The amendments in ASU 2020-06 further revise the guidance in *ASC 260, Earnings Per Share*, to require entities to calculate diluted earnings per share, or EPS, for convertible instruments by using the if-converted method. In addition, entities must presume share settlement for purposes of calculating diluted EPS when an instrument may be settled in cash or shares. ASU 2020-06 is effective for public business entities for annual reporting periods, and interim reporting periods within those annual periods, beginning after December 15, 2021 on a prospective basis, and early adoption is permitted. The Company is currently evaluating the impact this guidance will have on its financial statements.

NOTE 3. FAIR VALUE MEASUREMENTS AND FAIR VALUE OF FINANCIAL INSTRUMENTS

The fair value of the Company's financial assets and liabilities are determined in accordance with the fair value hierarchy established in FASB's ASC Topic 820, *Fair Value Measurements and Disclosures,* or Topic 820. Topic 820 defines fair value 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. The fair value hierarchy of Topic 820 requires an entity to maximize the use of observable inputs when measuring fair value and classifies those inputs into three levels:

Level 1—Observable inputs, such as quoted prices in active markets;

Level 2—Inputs, other than the quoted prices in active markets, which are observable either directly or indirectly such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the instrument's anticipated life; and

Level 3—Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

Our financial instruments consist primarily of cash and cash equivalents, short-term and long-term investments, accounts payable, the Loan and Security Agreement, or Term Loan, entered into with Hercules Capital Inc., or Hercules, and the Convertible Senior Notes.

Cash, cash equivalents and investments are reported at their respective fair values on Company's balance sheets. Where quoted prices are available in an active market, securities are classified as Level 1. The Company classifies money market funds and U.S. Treasury securities as Level 1. When quoted market prices are not available for the specific security, then the Company estimates fair value by using quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets. Where applicable, these models project future cash flows and discount the future amounts to a present value using market-based observable inputs obtained from various third-party data providers, including but not limited to benchmark yields, reported trades and broker/dealer quotes. Where applicable, the market approach utilizes prices and information from market transactions for similar or identical assets. The Company classifies U.S. government agency securities, commercial paper, corporate debt securities and asset-backed securities as Level 2. The Company's short-term and long-term investments are classified as available-for-sale.

The following tables set forth the value of the Company's financial assets remeasured on a recurring basis based on the three-tier fair value hierarchy by significant investment category as of December 31, 2020 and 2019.

	December 31, 2020						
					Reported as:		
(in thousands)	**Amortized Cost**	**Gross Unrealized Gains**	**Gross Unrealized Losses**	**Fair Value**	**Cash and Cash Equivalents**	**Short-term Investments**	**Long-term investments**
Cash	$ 2,011	$ —	$ —	$ 2,011	$ 2,011	$ —	$ —
Level 1:							
Money market fund	25,862	—	—	25,862	25,862	—	—
U.S. Treasury securities	8,157	1	(1)	8,157	—	8,157	—
Subtotal	34,019	1	(1)	34,019	25,862	8,157	—
Level 2:							
U.S. government agency securities	64,370	15	(3)	64,382	—	41,625	22,757
Commercial paper	159,183	16	(6)	159,193	97,989	61,204	—
Corporate debt securities	72,546	134	(1)	72,679	11,995	60,684	—
Subtotal	296,099	165	(10)	296,254	109,984	163,513	22,757
Total assets measured at fair value	$ 332,129	$ 166	$ (11)	$ 332,284	$ 137,857	$ 171,670	$ 22,757

(in thousands)	December 31, 2019 Amortized cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value	Reported as: Cash and Cash Equivalents	Short-term Investments	Long-term investments
Cash	$ 1,393	$ —	$ —	$ 1,393	$ 1,393	$ —	$ —
Level 1:							
Money market fund	17,181	—	—	17,181	17,181	—	—
Level 2:							
U.S. Government agency securities	40,741	6	(14)	40,733	—	19,990	20,743
Commercial paper	108,248	107	(2)	108,353	—	108,353	—
Corporate debt securities	185,569	205	(20)	185,754	—	159,517	26,237
Asset-backed securities	1,561	3	—	1,564	—	1,564	—
Subtotal	336,119	321	(36)	336,404	—	289,424	46,980
Total assets measured at fair value	$ 354,693	$ 321	$ (36)	$ 354,978	$ 18,574	$ 289,424	$ 46,980

Interest income related to the Company's cash, cash equivalents and available-for-sale investments included in other income (expense), net was approximately $4.4 million, $8.7 million and $3.5 million for the years ended December 31, 2020, 2019 and 2018, respectively. There were $34 thousand gross realized gains on the sale of available-for-sale investments for the year ended December 31, 2020, and there were no gross realized gains and gross realized losses for the years ended 2019 and 2018.

The following table summarizes the Company's available-for-sale investments that were in a continuous unrealized loss position but not deemed due to credit losses and therefore not required to be charged to earnings against the allowance for expected credit losses, as of December 31, 2020 and 2019.

(in thousands)	December 31, 2020 Fair Value	December 31, 2020 Unrealized Losses	December 31, 2019 Fair Value	December 31, 2019 Unrealized Losses
U.S. Treasury securities	$ 6,143	$ (1)	$ —	$ —
U.S. government agency securities	16,496	(3)	24,235	(14)
Commercial paper	24,713	(6)	5,426	(2)
Corporate debt securities	18,012	(1)	38,668	(20)
Total	$ 65,364	$ (11)	$ 68,329	$ (36)

The Company held a total of 12 and 18 positions which were in an unrealized loss position as of December 31, 2020 and 2019, respectively. All available-for-sale investments in an unrealized loss position were in a continuous loss position for less than 12 months. The Company determined that there was no allowance for expected credit losses related to our available-for-sale investments as of December 31, 2020 because the Company does not believe that it will be required to sell these securities before the recovery of their amortized cost basis.

The following table summarizes the maturities of the Company's available-for-sale investments (excluding money market funds), as of December 31, 2020.

(in thousands)	December 31, 2020 Amortized Cost	December 31, 2020 Fair Value
Mature in less than one year	$ 281,508	$ 281,654
Mature in one to five years	22,748	22,757
Total	$ 304,256	$ 304,411

The following table presents a reconciliation of financial liabilities measured at fair value on a recurring basis using Level 3 unobservable inputs for the year ended December 31, 2020 and 2019.

	Years Ended December 31,	
	2020	2019
(in thousands)	Compound Derivative Liability	Compound Derivative Liability
Fair value at beginning of year	$ 977	$ 161
Change in fair value	(775)	816
Fair value at end of year	$ 202	$ 977

The following table presents information about significant unobservable inputs related to the Company's Level 3 financial liabilities as of December 31, 2020.

	December 31, 2020			
(in thousands)	Fair Value	Valuation Technique	Significant Unobservable Input	Input
Compound derivative liability	$ 202	Discounted cash flow	Discount rate	12.7 %
			Probability of the occurrence of certain events	20.0 %

The estimated fair value of the Term Loan was $76.1 million and $59.2 million as of December 31, 2020 and 2019, respectively, and is classified as Level 3. The key valuation assumptions used to calculate the fair value of the Term Loan as of December 31, 2020 consist of the discount rate of 12.7% and the probability of occurrence of certain events of 20.0%. The key valuation assumptions used to calculate the fair value of the Term Loan as of December 31, 2019 consist of the discount rate of 10.7% and the probability of occurrence of certain events of 20.0%.

The estimated fair value of the Convertible Senior Notes was $108.5 million as of December 31, 2020 and they were classified as Level 3. The key valuation assumptions used to calculate the fair value of the Convertible Senior Notes consist of the discount rate of 16.7% and volatility of 70.0%.

NOTE 4. LEASES

The Company accounts for leases under Topic 842, adopted as of January 1, 2019.

In July 2014, the Company entered into a five-year noncancelable operating lease for its offices and laboratory space in South San Francisco, California that was scheduled to expire in June 2019, with an option for the Company to extend the lease for an additional 3 years. In August 2017, the Company entered into an amendment which extended the existing operating lease to June 2021 and added 13,258 square feet of additional lease space resulting in a total of 26,987 square feet being leased in the aggregate under the amended lease. In November 2017, the Company entered into a second amendment which reduced the common areas resulting in a total of 26,897 square feet being leased in aggregate under the second amendment.

On August 14, 2019, the Company entered into a third amendment to the existing operating lease which extended the leased space by an additional 19,177 square feet, or Second Expansion Premises, which resulted in a total of 46,074 square feet being leased in aggregate. In conjunction with the third amendment, the Company also agreed to lease 5,569 square feet of temporary office space from August 15, 2019 through the commencement date of the Second Expansion Premises. The third amendment extended the lease by 84 months from the Second Expansion Premises commencement date, with an option to extend the lease for an additional 36 months subject to certain conditions. The Company determined that the Second Expansion Premises would be accounted for as a new lease at the commencement date of the Second Expansion Premises. Further, the Company determined that the amendment to the existing operating lease and temporary office space would be accounted as a lease modification upon execution of the third amendment. In December 2020, the Company entered into a fourth amendment to the existing operating lease which, among other things, confirmed the commencement date of the Second Expansion Premises to be September 1, 2020. The Company recognized an operating lease right-of-use, or ROU, asset of $8.1 million and operating lease liability of $8.1 million on its balance sheet upon the execution of the third amendment on August 14, 2019, and measured and recorded an additional ROU asset of $5.8 million and operating lease liability of $5.8 million for the Second Expansion Premises upon the Second Expansion Premises commencement date of September 1, 2020.

Operating lease expense was $2.2 million, $1.3 million and $1.0 million for the years ended December 31, 2020, 2019 and 2018, respectively. Expense related to short-term leases was not significant for the years ended December 31, 2020, 2019 and 2018. Variable lease cost was $0.7 million and $0.8 million for the years ended December 31, 2020 and 2019, respectively. Operating cash flows for the year ended December 31, 2020 and 2019 included $1.3 million and $1.1 million in cash payments for operating leases, respectively.

The following table presents the maturity analysis of the Company's operating lease liabilities showing the aggregate lease payments as of December 31, 2020.

(in thousands)	December 31, 2020
2021	$ 2,171
2022	2,847
2023	2,933
2024	3,020
2025	3,111
2026 and thereafter	5,383
Total lease payments	19,465
Less: imputed interest	(4,340)
Total operating lease liabilities	$ 15,125

Operating lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. In determining the present value of lease payments, the Company uses its incremental borrowing rate. The weighted average incremental borrowing rate used to determine the operating lease liabilities as of December 31, 2020 and December 31, 2019 was 7.4% and 6.0%, respectively. The Company's weighted average remaining lease term was 6.7 years and 7.7 years as of December 31, 2020 and December 31, 2019, respectively.

NOTE 5. OTHER BALANCE SHEET COMPONENTS

Property and Equipment, Net

The following table presents the components of property and equipment, net as of December 31, 2020 and 2019.

(in thousands)	December 31, 2020	December 31, 2019
Furniture and fixtures	$ 274	$ 265
Computer and lab equipment	3,277	3,867
Leasehold improvements	1,786	1,244
	5,337	5,376
Less: accumulated depreciation and amortization	(4,225)	(2,648)
Total property and equipment, net	$ 1,112	$ 2,728

Depreciation and amortization expense was approximately $0.9 million, $0.8 million and $0.6 million for the years ended December 31, 2020, 2019 and 2018, respectively.

Accrued Expenses and Other Current Liabilities

The following table presents the components of accrued expenses and other current liabilities as of December 31, 2020 and 2019.

(in thousands)	December 31, 2020	December 31, 2019
Accrued clinical and nonclinical study costs	$ 3,846	$ 8,343
Accrued contract manufacturing	15,511	17,343
Accrued compensation	2,231	3,367
Accrued interest	1,434	—
Accrued restructuring	4,856	—
Accrued professional fees and other	793	3,727
Total accrued expenses and other current liabilities	$ 28,671	$ 32,780

NOTE 6. BORROWINGS

Term Loan

On February 28, 2018, the Company entered into the Term Loan with Hercules. The Term Loan provided for a loan in an aggregate principal amount of up to $100.0 million to be funded in five tranches subject to certain performance-based milestones. The first tranche, in the amount of $25.0 million, was funded on the closing date of the Term Loan.

On October 15, 2018, the Company and Hercules entered into the second amendment to the Term Loan, which amended certain terms of the Term Loan. After giving effect to the second amendment, the Term Loan continued to provide for a loan in an aggregate principal amount of up to $100.0 million to be funded in five tranches subject to certain performance-based milestones. The second tranche was reduced from $25.0 million to $15.0 million and was funded on December 28, 2018. The Company accounted for the second amendment as a modification to the existing Term Loan.

On March 27, 2019, the Company modified the Term Loan with Hercules by entering into the third amendment to the Term Loan. After giving effect to the third amendment, the amount available under the Term Loan is increased from up to $100.0 million to up to $200.00 million to be funded in tranches, subject to certain performance-based milestones, and the maturity of the Term Loan is extended. Under the terms of the Term Loan, as amended by the third amendment, the $40.0 million principal outstanding under the Term Loan at the date of the modification remains outstanding, and additional tranches of $20.0 million and $15.0 million will be available for draw down prior to December 15, 2019 and December 15, 2020, respectively. An additional tranche of $75.0 million was to be available for draw down between January 1, 2020 and December 15, 2020, on the condition that the Company obtain final approval from the U.S. Food and Drug Administration, or FDA, for the New Drug Application, or NDA, for veverimer. A final tranche of $50.0 million was to be available for draw down on or prior to December 15, 2021, upon request by the Company and the approval of Hercules' investment committee. The Company accounted for the third amendment as a modification to the existing Term Loan. On December 13, 2019, the third tranche of the Term Loan was funded in the amount of $20.0 million.

On March 31, 2020, the Company and Hercules entered into the fourth amendment to the Term Loan. After giving effect to the fourth amendment, the fourth tranche of amount $15.0 million previously under Hercules Capital, Inc. was split between two lenders, $5.0 million under Hercules Capital, Inc. and $10.0 million under Hercules Technology III, L.P. The Company accounted for the fourth amendment as a modification to the existing Term Loan.

On May 18, 2020, the Company and Hercules entered into the fifth amendment to the Term Loan. After giving effect to the fifth amendment, the additional tranche of $75.0 million was split into two separate tranches of $25.0 million and $50.0 million. The $25.0 million tranche was to be available for draw down between January 1, 2020 and December 15, 2020, on the condition that the Company obtained final approval from the FDA of the NDA for veverimer on or before December 15, 2020. The $50.0 million tranche was to be available for draw down between January 1, 2021 and June 30, 2021, on the condition that the $25.0 million tranche had been drawn and final approval had been received for the NDA for veverimer on or before December 15, 2020. A final tranche of $50.0 million was to be available for draw down on or prior to December 15, 2021, upon request by the Company and the approval of Hercules' investment committee. The fifth amendment also permits the issuance by the Company of certain convertible notes and cash payments to redeem or settle such convertible notes in accordance with the terms thereof. Such cash settlement or redemption is subject to a requirement that the Company maintain unrestricted cash in an amount not less than 100% of the outstanding obligations under the Term Loan from and after any such cash settlement or redemption, and that there be no default or event of default under the Term Loan at the time of such cash settlement or redemption. On May 19, 2020, the fourth tranche of the Term Loan was funded in the amount of $15.0 million.

The Term Loan bears interest at a floating per annum interest rate equal to the greater of either (i) 8.35% or (ii) the lesser of (x) 8.35% plus the prime rate as reported in The Wall Street Journal minus 6.00% and (y) 9.85%. The maturity date of the Term Loan is April 1, 2023 and the Company will initially be making interest-only payments until April 1, 2021. Upon expiration of the interest-only period, the Company will repay the Term Loan in equal monthly installments comprised of principal and interest, based on a 30-month amortization schedule, through maturity. The Company will pay an additional amount of (a) $2.6 million due on March 1, 2022 and (b) the product of 7.55% and the aggregate loans funded under the Term Loan due at maturity or on any earlier date on which the loans become due. If the Company prepays the Term Loan, the Company will be required to pay a prepayment charge equal to (i) 2.00% of the amount being prepaid at any time during the first 12 months following the effective date of the third amendment (ii) 1.50% of the amount being prepaid after 12 months but prior to 24 months following the effective date of the third amendment (iii) 1.00% of the amount being prepaid after 24 months but prior to 36 months following the effective date of the third amendment and (iv) zero if prepaid any time after 36 months following the effective date of the third amendment but prior to the maturity.

On January 6, 2021, the Company and Hercules entered into the sixth amendment to the Term Loan. The sixth amendment provides for, among other things, a decrease in the amount available under the Term Loan from $200.0 million to $75.0 million. The loan repayment schedule provides for interest only payments until April 1, 2022, followed by consecutive equal monthly amortization payments of principal and interest through the maturity date. The maturity date of the Loan Agreement is October 1, 2023, subject to extension to April 1, 2024 on the condition that the Company obtains final approval from the FDA for the NDA for veverimer on or before October 1, 2023. The sixth amendment also eliminates prepayment charges for prepayments of principal of the Term Loan made on or after March 1, 2021. The Company is currently evaluating the accounting for the sixth amendment to the Term Loan.

The Term Loan is secured by substantially all of the Company's assets, except its intellectual property, which is the subject of a negative pledge; however, the collateral does consist of rights to payments and proceeds from the sale, licensing or disposition of all or any part of, or rights in, its intellectual property. Under the Term Loan, the Company is subject to certain covenants, including but not limited to requirements to deliver financial reports at designated times of the year and maintain a minimum level of cash. These covenants also limit or restrict the Company's ability to incur additional indebtedness or liens, acquire, own or make any investments, pay cash dividends, repurchase stock or enter into certain corporate transactions, including mergers and changes of control.

Warrants

In conjunction with the Term Loan entered into on February 28, 2018, the Company issued a warrant to Hercules to purchase 53,458 shares of its common stock with an exercise price of $9.35 per share. The estimated fair value of the warrant at the date of issuance was approximately $0.2 million. The fair value of the common stock warrant liability was determined using the probability-weighted expected return method. It was recorded at its fair value at inception and was remeasured at each financial reporting period with any changes in fair value being recognized as a component of other income (expense), net in the accompanying statements of operations and comprehensive loss.

On April 10, 2018, the Company entered into amendments with Hercules that resulted in the reclassification of the warrant liability to stockholders' equity as the amended terms of the warrants qualified for them to be accounted for as equity instruments and as such were no longer subject to remeasurement. The fair value of the common stock warrants of approximately $0.2 million was reclassified to stockholders' equity upon execution of the amendment.

In connection with the funding of the second tranche on December 28, 2018, the Company issued to Hercules a warrant to purchase 53,458 shares of its common stock at an exercise price of $9.35 per share. The common stock warrant was recorded in stockholders' equity at its fair value of approximately $0.9 million on December 28, 2018.

In conjunction with the third amendment, the Company issued warrants to Hercules to purchase 16,721 shares of its common stock with an exercise price of $23.92 per share. The common stock warrants were recorded in stockholders' equity at their fair value of approximately $0.3 million on March 27, 2019. The fair value of the common stock warrants were determined using an option-pricing model with the following assumptions: time to liquidity of 7.0 years, volatility of 75.0%, risk-free rate of 2.3% and stock price based on the March 27, 2019 closing price of the Company's common stock reported by The Nasdaq Global Select Market.

In connection with the funding of the third tranche on December 13, 2019, the Company issued to Hercules a warrant to purchase 8,361 shares of its common stock at an exercise price of $23.92 per share. The common stock warrant was recorded in stockholders' equity at its fair value of approximately $0.3 million on December 13, 2019. The fair value of the common stock warrants was determined using an option-pricing model with the following assumptions: time to liquidity of 7.0 years, volatility of 72.7%, risk-free rate of 1.8% and stock price based on the December 13, 2019 closing price of the Company's common stock reported by The Nasdaq Global Select Market.

In connection with the funding of the fourth tranche on May 19, 2020, the Company issued Hercules and Hercules Technology III, L.P. warrants to purchase a total of 6,270 shares of its common stock at an exercise price of $23.92 per share. The common stock warrant was recorded in stockholders' equity at its fair value of approximately $0.1 million on May 19, 2020. The fair value of the common stock warrants was determined using an option-pricing model with the following assumptions: time to liquidity of 7 years, volatility of 69.9%, risk-free rate of 0.5% and stock price based on the May 19, 2020 closing price of the Company's common stock reported by The Nasdaq Global Select Market.

In connection with each subsequent draw down under the tranches described above, the Company is obligated to issue additional warrants to purchase a number of shares of the Company's common stock determined by dividing (x) an amount equal to 1.0% of the principal amount of the applicable tranche by (y) $23.92 subject to adjustments following certain corporate events.

On July 17, 2020, Hercules and Hercules Technology III, L.P. exercised warrants to purchase 85,533 and 21,383 shares, respectively, of the Company's common stock at an exercise price of $9.35 per share. A total of 68,816 shares of the Company's common stock was issued to Hercules and Hercules Technology III, L.P. in a net settlement transaction.

Embedded Derivatives and Other Debt Issuance Costs

The Company determined that certain loan features were embedded derivatives requiring bifurcation and separate accounting. Those embedded derivatives were bundled together as a single, compound embedded derivative and then bifurcated and accounted for separately from the host contract. The Company initially recorded a compound derivative liability of $0.7 million, which is required to be marked to market in future periods.

As of December 31, 2020, the Company calculated the fair values of the compound derivative using the “with and without” method under the income approach by computing the difference between the fair value of the Term Loan with the compound derivative and the fair value of the Term Loan without the compound derivative. The Company calculated the fair values using a probability-weighted discounted cash flow analysis. The key valuation assumptions used consist of the discount rate of 12.7% and the probability of the occurrence of certain events of 20%. The compound derivative liability is being remeasured at each financial reporting period with any changes in fair value being recognized as a component of other income (expense), net in the statements of operations and comprehensive loss. The fair value of the compound derivative liability was approximately $0.2 million and was classified as other long-term liabilities on the balance sheet.

The facility fee, fair value of warrants at issuance, fair value of embedded derivatives which were bifurcated, and other debt issuance costs have been treated as debt discounts on the Company’s balance sheet and together with the additional payment are being amortized to interest expense throughout the life of the Term Loan using the effective interest rate method.

As of December 31, 2020 and 2019, there were unamortized issuance costs and debt discounts of $2.3 million and $3.6 million, respectively, which were recorded as a direct deduction from the Term Loan on the balance sheets.

The following table presents future payments of principal and interest on the Term Loan as of December 31, 2020.

(in thousands)	December 31, 2020
2021	$ 26,574
2022	33,344
2023	24,867
	84,785
Less: amount representing interest	(9,785)
Present value of Term Loan	75,000
Less: current portion(1)	—
Long-term portion of Term Loan	$ 75,000

(1) The sixth amendment to the Term Loan executed on January 6, 2021 provides for interest only payments until April 1, 2022.

Convertible Senior Notes

On May 22, 2020, the Company issued $200.0 million aggregate principal amount of 3.50% convertible senior notes due 2027, or Convertible Senior Notes, pursuant to an indenture, dated as of May 22, 2020, or the Indenture, between the Company and U.S. Bank National Association, as trustee, or the Trustee. The offering and sale of the Convertible Senior Notes were made by the Company to the initial purchasers in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act of 1933, as amended, or the Securities Act, for resale by the initial purchasers to qualified institutional buyers (as defined in the Securities Act) pursuant to the exemption from registration provided by Rule 144A under the Securities Act. The issuance includes the exercise in full by the initial purchasers of their option to purchase an additional $25.0 million aggregate principal amount of Convertible Senior Notes. Net proceeds from the offering were $193.3 million after deducting underwriting discounts and commissions and other offering costs of approximately $6.7 million.

The Convertible Senior Notes are senior unsecured obligations of the Company, and interest is payable semi-annually in arrears on May 15 and November 15 of each year, beginning on November 15, 2020. The Convertible Senior Notes mature on May 15, 2027, unless earlier repurchased, redeemed or converted and are not redeemable prior to May 20, 2024. The Company may redeem for cash all or any portion of the Convertible Senior Notes, at the Company's option, on or after May 20, 2024 and on or before the 40th scheduled trading day immediately prior to the maturity date, if the last reported sale price of the Company's common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive), including the trading day immediately preceding the date on which the Company provides notice of redemption, during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which the Company provides notice of redemption at a redemption price equal to 100% of the principal amount of the Convertible Senior Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. The Company has not provided a sinking fund for the Convertible Senior Notes, nor is one required to be provided.

The Convertible Senior Notes are convertible into cash, shares of the Company's common stock or a combination of cash and shares of the Company's common stock at the Company's election at an initial conversion rate of 30.0978 shares of the Company's common stock per $1,000 principal amount of the Convertible Senior Notes, which is equivalent to an initial conversion price of approximately $33.23 per share of the Company's common stock. The conversion rate is subject to customary adjustments for certain events as described in the Indenture. It is the Company's current intent to settle conversions through combination settlement, which involves repayment of the principal portion in cash and any excess of the conversion value over the principal amount in shares of its common stock. As of December 31, 2020, the "if-converted value" did not exceed the remaining principal amount of the Convertible Senior Notes.

Holders may convert their Convertible Senior Notes, at their option, prior to the close of business on the business day immediately preceding February 15, 2027, only under the following circumstances:

- during any fiscal quarter commencing after the calendar quarter ending on September 30, 2020, if the last reported sale price of the Company's common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;

- during the five consecutive business day period immediately following any ten consecutive trading day period, or the Measurement Period, in which the trading price per $1,000 principal amount of the Convertible Senior Notes, as determined following a request by a holder of notes in accordance with certain procedures described in the Indenture, for each trading day of the Measurement Period was less than 98% of the product of the last reported sales price of the Company's common stock and the conversion rate on each such trading day;

- upon the occurrence of certain corporate events or distributions of the Company's common stock, as described in the Indenture;

- after the Company's issuance of a notice of redemption; or

- at any time from, and including, February 15, 2027 until the close of business on the trading day immediately before the maturity date.

If the Company undergoes a fundamental change, as described in the Indenture, subject to certain conditions, holders may require the Company to repurchase for cash all or any portion of their Convertible Senior Notes. The fundamental change repurchase price is equal to 100% of the principal amount of the Convertible Senior Notes to be repurchased, plus accrued and unpaid interest up to, but excluding, the fundamental change repurchase date. In addition, following certain corporate events that occur prior to the maturity date or if the Company delivers a notice of redemption, the Company will increase, in certain circumstances, the conversion rate for a holder who elects to convert its Convertible Senior Notes in connection with such a corporate event or notice of redemption, as the case may be.

The Convertible Senior Notes are the Company's senior unsecured obligations and rank senior in right of payment to any of the Company's indebtedness that is expressly subordinated in right of payment to the Convertible Senior Notes; equal in right of payment to any of the Company's unsecured indebtedness that is not so subordinated; effectively subordinated in right of payment to any of the Company's secured indebtedness, including secured indebtedness under the Term Loan, to the extent of the value of the assets securing such indebtedness; and structurally subordinated to all indebtedness and other liabilities (including trade payables) of the Company's future subsidiaries, if any.

The Indenture contains customary events of default with respect to the Convertible Senior Notes and provides that upon certain events of default occurring and continuing, the trustee may, and the trustee at the request of holders of at least 25% in principal amount of the Convertible Senior Notes shall declare all principal and accrued and unpaid interest, if any, of the Convertible Senior Notes to be due and payable. In case of certain events of bankruptcy, insolvency or reorganization, involving the Company or a significant subsidiary, all of the principal of and accrued and unpaid interest on the Convertible Senior Notes will automatically become due and payable.

At issuance, the Convertible Senior Notes were bifurcated into liability and equity components and accounted for separately. The carrying amount of the liability component was calculated to be $117.7 million by measuring the fair value of similar debt instruments that do not have an associated convertible feature. The carrying amount of the equity component, representing the conversion option, was determined by deducting the fair value of the liability component from the par value of the Convertible Senior Notes. The carrying amount of the equity component was calculated to be $82.3 million and was recorded in additional paid-in capital. The equity component is not remeasured as long as it continues to meet the conditions for equity classification. The allocation of proceeds into the equity component resulted in a debt discount for the Convertible Senior Notes that is amortized to interest expense at an effective interest rate of 13.5% over the effective life of the Convertible Senior Notes of 7 years, using the effective interest method.

Underwriter discounts and issuance costs of $6.7 million were allocated to the liability and equity components based on the proportion of proceeds allocated to the debt and equity components. Underwriter discounts and issuance costs allocated to the liability component were $4.0 million and are amortized to interest expense over the term of the Convertible Senior Notes using the effective interest method. Underwriter discounts and issuance costs attributable to the equity component were $2.7 million and are netted against the equity component in additional paid-in capital.

The following table presents the carrying amount of the liability and equity components of the Convertible Senior Notes as of December 31, 2020.

(in thousands)		December 31, 2020
Liability component:		
Principal	$	200,000
Unamortized discount - equity component		(77,503)
Unamortized underwriter discounts and issuance costs		(3,827)
Net carrying amount	$	118,670
Equity component, net of underwriter discounts and issuance costs	$	79,498

The remaining unamortized debt discount will be amortized over approximately 6.5 years which is also the remaining life of the Senior Convertible Notes.

The following table presents the interest expense related to the Convertible Senior Notes for the year ended December 31, 2020.

(in thousands)		Year Ended December 31, 2020
Contractual interest expense	$	4,258
Amortization of debt discount		4,757
Amortization of underwriter discounts and issuance costs		126
Total interest expense	$	9,141

NOTE 7. COMMITMENTS AND CONTINGENCIES

The Company has contractual obligations from its operating lease, manufacturing and service contracts, Term Loan and tenant improvement loan, and other research and development activities. The following table aggregates the Company's material expected contractual obligations and commitments as of December 31, 2020.

	December 31, 2020				
(in thousands)	Total	2021	2022 - 2023	2024 - 2025	Thereafter
Term Loan[(1)]	$ 93,067	$ 26,574	$ 66,493	$ —	$ —
Convertible Senior Notes[(2)]	245,500	7,000	14,000	14,000	210,500
Lease obligations[(3)]	19,465	2,171	5,780	6,131	5,383
Tenant improvement loan	47	47	—	—	—
Manufacturing and service contracts[(4)]	566,375	50,961	119,432	121,840	274,142
Total contractual obligations and commitments	$ 924,454	$ 86,753	$ 205,705	$ 141,971	$ 490,025

(1) Comprised of amounts due under the fifth amendment to the Term Loan executed on May 18, 2020. The sixth amendment to the Term Loan executed on January 6, 2021 provides for interest only payments until April 1, 2022.
(2) Comprised of interest payable and principal repayment due under the Convertible Senior Notes' Indenture.
(3) Comprised of the rent payments under the amended lease executed on August 14, 2019.
(4) The purchase obligations are comprised of our non-cancelable purchase commitments under our Manufacturing and Commercial Supply Agreement with Patheon. These amounts are based on forecasts that may include estimates of our future market demand, quantity discounts and manufacturing efficiencies.

Facilities

The Company has an operating lease for its offices and laboratory space in South San Francisco. See Note 4. "Leases" for additional information about this lease.

Other Commitments

On October 4, 2019, the Company and Patheon entered into a multi-year Manufacturing and Commercial Supply Agreement, or the Supply Agreement, under which Patheon agreed to manufacture and supply veverimer to support the Company's commercialization efforts. Patheon has also agreed to manufacture and supply veverimer to support the Company's drug development and clinical trial activities. Under the Supply Agreement, the Company is obligated to make certain purchases of drug substance. The Company and Patheon are also parties to a Master Development/Validation Services and Clinical/Launch Supply Agreement, or the MDA, pursuant to which Patheon agreed to manufacture and supply veverimer. Certain manufacturing activities previously governed by the MDA are now subject to the Supply Agreement, whereas other ongoing manufacturing activities under the MDA will continue to be governed by the MDA until such activities are complete.

The Supply Agreement may be terminated by either party following an uncured material breach by the other party, in the event the other party becomes insolvent or subject to bankruptcy proceedings, or in connection with a force majeure event that continues beyond 12 months. In addition, the Supply Agreement may be terminated by the Company upon the occurrence of certain regulatory events or actions, including: (i) if the Company does not obtain regulatory approval for veverimer by a specified date or (ii) if the Company terminates its commercialization of veverimer or fails to launch veverimer by a specified date. The Company's obligation to purchase veverimer is subject to minimum and maximum annual commitments, with the minimum commitments subject to reduction in certain circumstances. Patheon has agreed to make facility improvements under the Supply Agreement and will be the exclusive owner of the purchased equipment and facility improvements. Patheon may manufacture other products with the facility improvements when not occupied by manufacturing veverimer. Under the Supply Agreement, the Company has agreed to reimburse Patheon up to a specified amount for plant modifications. These payments were expensed to research and development expense.

The Company also enters into other contracts in the normal course of business with contract research organizations, contract development and manufacturing organizations and other service providers and vendors. These contracts generally provide for termination on short notice and are cancelable contracts and accordingly, are not included in the contractual obligations and disclosures summarized above.

Contingencies

On January 6, 2021, a putative securities class action was filed in the U.S. District Court for the Northern District of California against the Company and its CEO and CFO (the "Securities Class Action"). Pardi v. Tricida, Inc., et al., 21-cv-00076. The Securities Class Action complaint alleges that during the period September 4, 2019 through October 28, 2020 (the "Class Period"), the Company and its senior officers violated the federal securities laws, including under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder, through alleged public misrepresentations and/or omissions of material facts concerning the Company's NDA for veverimer and the likelihood and timing of approval of veverimer by the FDA. No damages amount is specified in the Securities Class Action.

On February 15, 2021, a derivative action was filed in the District of Delaware, brought by and on behalf of Tricida, Inc. as a Nominal Defendant, against the Company's directors as well as its CEO and CFO (the "Derivative Case"). Ricks v. Alpern et al., Case No, 1:21-cv-000205. The Derivative Case is based on the allegations of the Securities Class Action and asserts that by allowing the Company and senior executives to make the allegedly false and misleading statements at issue in the Securities Class Action, the defendants breached their fiduciary duties and wasted corporate assets. Additionally, the complaint asserts claims against the senior officers for violation of Sections 10(b) and 21D of the Securities Exchange Act of 1934. No damages amount is specified in the Derivative Case.

At this time, the Company has not provided for a loss contingency in its financial statements relating to the Securities Class Action and the Derivative Case since it is not probable that a loss has been incurred.

While there are no material legal proceedings the Company is aware of, the Company may become party to various claims and complaints arising in the ordinary course of business. Management does not believe that any ultimate liability resulting from any of these claims will have a material adverse effect on its results of operations, financial position, or liquidity. However, management cannot give any assurance regarding the ultimate outcome of these claims, and their resolution could be material to operating results for any particular period, depending upon the level of income for the period.

Guarantees and Indemnifications

The Company indemnifies each of its directors and officers for certain events or occurrences, subject to certain limits, while the director is or was serving at the Company's request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws. The term of the indemnification period lasts as long as a director may be subject to any proceeding arising out of acts or omissions of such director in such capacity. The maximum amount of potential future indemnification is unlimited; however, the Company currently holds director liability insurance. This insurance allows the transfer of risk associated with the Company's exposure and may enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, it has not recognized any liabilities relating to these obligations for any period presented.

NOTE 8. STOCKHOLDERS' EQUITY

On July 2, 2018, the Company's amended and restated certificate of incorporation became effective, authorizing the Company to issue a total of 440,000,000 shares of all classes of capital stock, consisting of 400,000,000 shares of common stock, par value $0.001 per share, and 40,000,000 shares of preferred stock, par value $0.001 per share. As of December 31, 2020 and 2019, the Company had 50,210,779 and 49,763,176 shares of common stock outstanding, respectively. As of December 31, 2020 and 2019, the Company had no shares of preferred stock outstanding.

Common Stock

On July 2, 2018, the Company completed its IPO and issued 13,455,000 shares of common stock at an offering price of $19.00 per share for net proceeds of approximately $237.7 million, after deducting underwriting discounts and commissions of $17.9 million. Upon the closing of the IPO, all of the 104,225,638 shares of convertible preferred stock outstanding were automatically converted on a 1:3.98 basis into 26,187,321 shares of common stock.

On April 8, 2019, the Company consummated an underwritten public offering and issued 6,440,000 shares of common stock, which included the exercise in full by the underwriters of their option to purchase 840,000 additional shares of common stock at an offering price of $36.00 per share for net proceeds of approximately $217.9 million, after deducting underwriting discounts and commissions of $13.9 million.

Common stock reserved for future issuance as of December 31, 2020 and 2019, consisted of the following.

	December 31, 2020	December 31, 2019
Stock options and RSUs issued and outstanding	8,120,435	6,809,257
Stock options, RSUs and ESPP shares authorized for future issuance	4,053,582	3,257,316
Total	12,174,017	10,066,573

NOTE 9. STOCK-BASED COMPENSATION

Equity Incentive Plans

During 2013, the Company adopted an equity compensation plan, the 2013 Equity Incentive Plan, or 2013 Plan, for eligible employees, officers, directors, advisors, and consultants. The 2013 Plan provided for the grant of incentive and non-statutory stock options. In June 2018, the Company's board of directors and stockholders approved the 2018 Equity Incentive Plan, or 2018 Plan. Any shares of common stock covered by awards granted under the 2013 Plan that terminated after June 22, 2018 by expiration, forfeiture, or cancellation were added to the 2018 Plan reserve and shares available for future issuance under the 2013 Plan were canceled.

The initial number of shares of common stock available for issuance under the 2018 Plan was 4,000,000. Unless our board of directors provides otherwise, beginning on January 1, 2019 and continuing until the expiration of the 2018 Plan, the total number of shares of common stock available for issuance under the 2018 Plan will automatically increase annually on January 1 by the lesser of (i) 3,200,000 shares of Common Stock, (ii) 4% of the total number of issued and outstanding shares of common stock as of December 31 of the immediately preceding year and (iii) an amount determined by the board of directors. Under the 2018 Plan, any shares that are forfeited or expired are added back to the shares available for issuance. In the year ended December 31, 2020, the number of shares of common stock reserved for issuance under the 2018 Plan was increased by 1,990,527 shares. As of December 31, 2020, 2,448,459 shares of common stock were available for future issuance of stock options and restricted stock and other stock-based awards under the 2018 Plan.

The terms of the stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the plans. Generally, stock options granted by the Company vest over a period of one to four years and are exercisable after they have been granted for up to 10 years from the date of grant. Under the Company’s 2013 Plan and 2018 Plan, the term of the option expires upon the earliest of: 1) termination of continuous service for cause; 2) three months after the termination of continuous service for reasons other than cause, death or disability; 3) 12 months after the termination of continuous service due to disability; 4) 18 months after the employee’s death if the employee died during the period of continuous service; 5) expiration date in the grant notice; or 6) the day before the tenth anniversary of the date of grant. The exercise price of the stock options must equal at least the closing price of the Company's common stock on the date of grant.

The 2013 Plan provides for early exercise where the stock option holders may exercise their stock options prior to vesting. Under the 2018 Plan, early exercise of stock options may be allowed on a grant by grant basis. Common stock that is issued upon the early exercise of options is subject to repurchase by the Company at the original exercise price at the option of the Company until the vesting date of the stock options. As of December 31, 2020, no shares of the Company's common stock were subject to repurchase. As of December 31, 2019, there were 5,040 shares of common stock that were subject to repurchase with an aggregate purchase price of approximately $17 thousand reflecting a weighted average price of $3.47 per share.

The following table summarizes stock option activity under the 2013 Plan and the 2018 Plan for the year ended December 31, 2020.

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term *(years)*	Aggregate Intrinsic Value *(thousands)*
Balance at December 31, 2019	6,797,983	$ 18.38	8.3	$ 133,892
Granted	4,543,304	26.37		
Exercised	(317,996)	3.46		
Forfeited or canceled	(2,992,876)	29.77		
Balance at December 31, 2020	8,030,415	$ 19.25	7.1	$ 10,137
Vested and expected to vest at December 31, 2020	7,613,776	$ 18.89	7.0	$ 10,122
Exercisable at December 31, 2020	7,166,917	$ 20.11	7.8	$ 10,377

Beginning in the year ended December 31, 2018, the Company began to issue restricted stock units, or RSUs, to directors under the 2018 Plan. Awards granted to directors vest on the earlier of the one-year anniversary of the award's date of grant or the date of the Company’s next annual meeting of stockholders that occurs following the date of grant. In addition, during the year ended December 31, 2020, the Company granted RSUs to certain employees as retention awards. These RSUs will vest on December 31, 2021.

The following table summarizes RSU activity under the 2018 Plan for the year ended December 31, 2020.

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance at December 31, 2019	11,274	$ 36.74
Granted	104,520	16.17
Vested	(11,274)	36.74
Forfeited	(14,500)	11.71
Unvested balance at December 31, 2020	90,020	$ 16.88

The total vest date fair value of RSUs vested in the year ended December 31, 2020 and 2019 were $0.4 million and $0.8 million, respectively. There were no RSUs that vested during year ended December 31, 2018.

Employee Stock Purchase Plan

In June 2018, the Company's board of directors and stockholders approved the Tricida Inc. ESPP, or ESPP. The ESPP allows eligible employees to have up to 15.0% of their eligible compensation withheld and used to purchase common stock, subject to a maximum of $25,000 worth of stock purchased in a calendar year or no more than 2,500 shares in an offering period, whichever is less. An offering period consists of a 6-month purchase period, with a look back feature to our stock price at the commencement of the offering period. Eligible employees can purchase the Company's common stock at the end of the offering period at 85.0% of the lower of the closing price of our common stock on The Nasdaq Global Select Market on the first and last day of the offering periods.

The initial number of shares of common stock available for issuance under the ESPP, was 800,000. Unless the Company's board of directors provides otherwise, beginning on January 1, 2019, the maximum number of shares which shall be made available for sale under the ESPP will automatically increase on the first trading day in January of each calendar year during the term of the ESPP by an amount equal to the lesser of (i) 1.0% of the total number of shares issued and outstanding on December 31 of the immediately preceding calendar year, (ii) 800,000 shares or (iii) an amount determined by the board of directors.

In the year ended December 31, 2020, the number of shares of common stock reserved for issuance under the ESPP was increased by 497,631 shares. The Company issued 51,444 shares under the ESPP, representing approximately $0.9 million in employee contributions, for the year ended December 31, 2020. As of December 31, 2020, there were 1,605,123 shares of common stock were available for future issuance under the ESPP.

Performance Awards

In August 2019, the Company granted 594,000 stock options under its 2018 Plan with a performance-based milestone with graded vesting over 18 months. In September 2020, the Company granted 868,500 stock options under the 2018 Plan with performance-based milestones with graded vesting over the estimated service period required to meet the performance-based targets. Compensation expense for performance-based awards is recorded over the estimated service period when the performance conditions are deemed probable of achievement. For the years ended December 31, 2020 and 2019, the stock compensation expense recorded was for performance conditions deemed probable of achievement and/or achieved.

Stock Option Valuation Assumptions

As stock-based compensation recognized is based on options ultimately expected to vest, the expense has been reduced for estimated forfeitures. The Company uses the Black-Scholes option pricing model to determine the estimated fair value of stock options at the date of the grant. The Black-Scholes model requires the input of subjective assumptions, including expected term, expected volatility, risk-free rate of return, expected dividend yield and the estimated fair value of the underlying common stock on the date of grant.

Expected Term: The expected term of the options represents the average period the stock options are expected to remain outstanding. As the Company does not have sufficient historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior, the expected term of options granted is derived from the average midpoint between the weighted average vesting term and the contractual term, also known as the simplified method.

Expected Volatility: Beginning in the fourth fiscal quarter of 2019, expected volatility is estimated using a weighted-average historical volatility for our common stock and the historical volatility of the common stock of a representative group of comparable publicly traded companies over a period equal to the expected term of the stock option grants. Prior to the fourth fiscal quarter of 2019, since the Company did not have sufficient trading history for its common stock, the expected volatility was based on the historical volatility of the common stock of comparable publicly traded companies. The Company selected companies with comparable characteristics, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the Company's stock-based awards.

Risk-Free Interest Rate: The risk-free interest rate is based on the yield of U.S. Treasury notes as of the grant date with terms commensurate with the expected term of the option.

Expected Dividends: The expected dividends assumption is based on the Company's expectation of not paying dividends in the foreseeable future.

The fair value of the stock options granted to employees for the years ended December 31, 2020, 2019 and 2018 was calculated with the following assumptions.

	Years Ended December 31,		
	2020	2019	2018
Risk-free interest rate	0.8 %	2.1 %	2.7 %
Expected volatility	69.9 %	73.6 %	64.6 %
Expected term (in years)	5.9	5.9	5.8
Expected dividends	— %	— %	— %

The fair value of the stock options granted to nonemployees for the years ended December 31, 2020, 2019 and 2018 was calculated with the following assumptions.

	Years Ended December 31,		
	2020	2019	2018
Risk-free interest rate	0.1 %	2.5 %	2.7 %
Expected volatility	80.5 %	76.4 %	68.4 %
Expected term (in years)	1.4	6.4	10.0
Expected dividends	— %	— %	— %

The following table summarizes the weighted-average fair value per share of stock options granted and the total intrinsic value of stock options exercised for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31,		
(in thousands, except per share amounts)	2020	2019	2018
Stock options granted - weighted-average grant date fair value per share	$ 16.21	$ 19.28	$ 10.39
Stock options exercised - intrinsic value	7,405	34,416	1,935

Stock-Based Compensation

The following table presents stock-based compensation expense as reported in the Company's statements of operations and comprehensive loss for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31,		
(in thousands)	2020	2019	2018
Research and development	$ 10,966	$ 13,547	$ 2,643
General and administrative	17,332	11,621	2,509
Total	$ 28,298	$ 25,168	$ 5,152

The following table presents stock-based compensation expense by award type as reported in the Company's statements of operations and comprehensive loss for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31,		
(in thousands)	2020	2019	2018
Stock options	$ 27,128	$ 24,271	$ 4,806
RSUs	776	447	202
ESPP	394	450	144
Total	$ 28,298	$ 25,168	$ 5,152

As of December 31, 2020, there was approximately $40.3 million of unrecognized stock-based compensation associated with stock options which the Company expects to recognize over a weighted-average period of 2.1 years. As of December 31, 2020, there was approximately $0.8 million of unrecognized stock-based compensation associated with RSUs which the Company expects to recognize over a weighted-average period of 0.8 years.

NOTE 10. RESTRUCTURING

Third Quarter 2020 Restructuring

In August 2020, the Company received a Complete Response Letter, or CRL, from the FDA related to its NDA for veverimer. Due to the resulting delay in regulatory approval and commercialization of veverimer, on September 10, 2020, the Compensation Committee of the Board of Directors approved the Tricida, Inc. 2020 Reduction in Force Severance Benefit Plan, or 2020 Restructuring Plan. On September 18, 2020, the Company implemented a restructuring, or Third Quarter 2020 Restructuring, under the 2020 Restructuring Plan to streamline the organization and preserve capital that included the elimination of approximately 21.5% of the Company's workforce as of September 18, 2020 and other cost reductions.

Following is a summary of accrued restructuring costs related to the Third Quarter 2020 Restructuring as of December 31, 2020.

(in thousands)	Severance and Benefits Costs	Contract Termination Costs	Total
Balance at January 1, 2020	$ —	$ —	$ —
Charges	2,524	136	2,660
Cash payments made	(2,456)	(137)	(2,593)
Non-cash and other adjustments	(6)	1	(5)
Balance at December 31, 2020	$ 62	$ —	$ 62

Restructuring costs of $2.4 million and $0.3 million were recorded in general and administrative expense and research and development expense, respectively, in our statements of operations and comprehensive loss during the year ended December 31, 2020.

Fourth Quarter 2020 Restructuring

On October 25, 2020, the Company's Board of Directors approved and on October 28, 2020, the Company implemented a restructuring under the 2020 Restructuring Plan, or Fourth Quarter 2020 Restructuring, to reduce operating costs and better align its workforce with the needs of its business following the completion of the Type A meeting with the FDA in October 2020. The Fourth Quarter 2020 Restructuring resulted in the elimination of approximately 60.0% of the Company's workforce as of October 28, 2020 and included one-time termination severance payments and other employee-related costs, and exit costs including contract termination costs and accelerated depreciation of capitalized software.

Following is a summary of accrued restructuring costs related to the Fourth Quarter 2020 Restructuring as of December 31, 2020.

(in thousands)	Severance and Benefits Costs	Contract Termination Costs	Other Associated Costs	Total
Balance at January 1, 2020	$ —	$ —	$ —	$ —
Charges	7,338	3,077	679	11,094
Cash payments made	(3,555)	(2,032)	—	(5,587)
Non-cash and other adjustments	—	(34)	(679)	(713)
Balance at December 31, 2020	$ 3,783	$ 1,011	$ —	$ 4,794

Restructuring costs of $10.2 million and $0.9 million were recorded in general and administrative expense and research and development expense, respectively, in our statements of operations and comprehensive loss during the year ended December 31, 2020.

NOTE 11. NET LOSS PER SHARE

The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders for the years ended December 31, 2020, 2019 and 2018.

(In thousands, except share and per share amounts)	Years Ended December 31, 2020	2019	2018
Numerator:			
Net loss	$ (264,791)	$ (176,813)	$ (102,808)
Denominator:			
Weighted average common shares outstanding	50,030,053	47,530,174	22,158,354
Less: weighted average shares subject to repurchase	(2,318)	(8,937)	(12,162)
Weighted average number of shares used in basic and diluted net loss per share	50,027,735	47,521,237	22,146,192
Net loss per share, basic and diluted	$ (5.29)	$ (3.72)	$ (4.64)

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive.

The following weighted-average outstanding common stock equivalents were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have been antidilutive.

	December 31, 2020	2019	2018
Warrants to purchase convertible preferred or common stock	31,352	131,998	106,916
Assumed conversion of Convertible Senior Notes	6,019,560	—	—
Common stock subject to repurchase	—	5,040	20,193
Options and RSUs issued and outstanding	8,120,435	6,809,257	4,599,307
Total	14,171,347	6,946,295	4,726,416

NOTE 12. INCOME TAXES

The Company did not record a provision or benefit for income taxes for the years ended December 31, 2020 and 2018, and recorded a tax benefit of $0.1 million for the year ended December 31, 2019. The significant components of the Company’s net deferred tax assets as of December 31, 2020 and 2019 are shown below.

(in thousands)	December 31, 2020	2019
Deferred tax assets		
Net operating loss carryforwards	$ 131,116	$ 82,252
Research and development credits	13,307	8,968
Capitalized assets	286	79
Accruals and reserves	1,463	651
Operating lease liabilities	3,183	2,070
Stock-based compensation	8,861	4,250
Gross deferred tax assets	158,216	98,270
Deferred tax liabilities		
Convertible Senior Notes basis difference	(16,310)	—
Operating lease right-of-use assets	(2,904)	(1,969)
Gross deferred tax liabilities	(19,214)	(1,969)
Total net deferred tax assets	139,002	96,301
Less: valuation allowance	(139,002)	(96,301)
Net deferred tax assets	$ —	$ —

A valuation allowance is established when it is more likely than not that a deferred tax asset will not be realized. As of December 31, 2020 and 2019, the Company's valuation allowance was $139.0 million and $96.3 million, respectively. The valuation allowance increased by $42.7 million for the year ended December 31, 2020. The increase in the 2020 valuation allowance was primarily due to the addition of the 2020 net operating loss carryforwards.

The following is a reconciliation between the U.S. federal income statutory tax rate and the Company’s effective tax rate for the years ended December 31, 2020, 2019 and 2018.

	Years Ended December 31, 2020	2019	2018
U.S. federal statutory rate	21.0 %	21.0 %	21.0 %
Stock-based compensation	(0.2)	2.2	(0.2)
Permanent adjustments	—	(0.1)	(0.1)
Change to valuation allowance	(22.5)	(25.9)	(21.9)
Research and development credits	1.6	2.8	1.3
Net unrealized gain on available-for-sale investments	—	0.1	—
Other	0.1	—	(0.1)
Effective tax rate	— %	0.1 %	— %

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (“CARES Act”) was enacted in response to the COVID-19 pandemic. The tax relief measures under the CARES Act for businesses include a five-year net operating loss carryback, suspension of annual deduction limitation of 80% of taxable income from net operating losses generated in a tax year beginning after December 31, 2017, changes in the deductibility of interest, acceleration of alternative minimum tax credit refunds, payroll tax relief, and a technical correction to allow accelerated deductions for qualified improvement property. The Company does not expect the provisions of the CARES Act will have a significant impact on its financial statements.

As of December 31, 2020, the Company had approximately $594.5 million of federal net operating losses available for future use. Federal net operating losses incurred prior to January 1, 2018 of approximately $89.1 million expire beginning in 2033 while federal net operating losses incurred after December 31, 2017 of approximately $505.4 million will have an indefinite carryforward period, subject to annual limitations. Federal research credits of approximately $12.4 million that are available for future use expire beginning in 2033.

At December 31, 2020, the Company also had approximately $89.6 million of state net operating losses available for future use that expire beginning in 2033 and state research credits of approximately $5.5 million that have no expiration date.

Utilization of the net operating loss carryforwards and the research and development credits carryforwards may be subject to an annual limitation due to ownership change limitations that may have occurred or that could occur in the future, as required by Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, as well as similar state provisions. An ownership change is, as a general matter, triggered by sales or acquisitions of the Company's stock in excess of 50.0% on a cumulative basis during a three-year period by persons or groups of persons owning 5.0% or more of our total equity value. If the Company had experienced an ownership change at any time since its formation, utilization of the net operating loss or research credit carryforwards would have been subject to an annual limitation under Section 382 of the Code. Such limitation is determined by first multiplying the value of the Company’s stock at the time of the ownership change by the applicable long-term and tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss or research credit carryforwards before utilization. In the fourth quarter of 2020, the Company completed a study to assess whether any ownership changes had occurred from the Company’s formation through June 30, 2020, and concluded that the Company may have experienced multiple ownership changes during this time. The annual limitation may have limited the Company’s ability to utilize net operating losses against taxable income in a given year for both federal and state purposes, however, remaining net operating losses and credits will be available in future years before expiration during their respective carryforward periods.

ASC Topic 740-10 prescribes a comprehensive model for the recognition, measurement, presentation and disclosure in financial statements of any uncertain tax positions that have been taken or expected to be taken on a tax return. As of December 31, 2020 and 2019, the Company had unrecognized tax benefits of $3.7 million and $2.5 million, respectively. The amount of unrecognized tax benefits is not expected to significantly change over the next twelve months. No amounts, outside of valuation allowance, would impact the effective tax rate on continuing operations. The gross unrecognized tax benefits activity for the years ended December 31, 2020, 2019 and 2018 is as follows.

	Years Ended December 31,		
(in thousands)	2020	2019	2018
Gross unrecognized tax benefits at beginning of year	$ 2,543	$ 1,297	$ 819
Additions for tax positions related to prior year	21	—	—
Decrease related to prior year tax provisions	—	—	—
Additions for tax positions related to current year	1,121	1,246	478
Gross unrecognized tax benefits at end of year	$ 3,685	$ 2,543	$ 1,297

It is the Company’s policy to include penalties and interest expense related to income taxes as a component of income tax expense as necessary. Management determined that no accrual for interest and penalties was required as of December 31, 2020.

The Company files income tax returns with federal tax authorities as well as various states tax authorities in the United States. The Company’s tax years from 2013 to 2020 will remain open for examination by the federal and state authorities for three and four years respectively, from the date of utilization of any net operating loss or tax credits. The Company is not currently subject to income tax examinations by any authority.

NOTE 13. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following presents certain unaudited quarterly financial information for the years ended December 31, 2020 and 2019. This information has been prepared on the same basis as the audited financial statements and includes all adjustments (consisting only of normal recurring adjustments) necessary to present fairly the unaudited quarterly results of operations set forth herein.

	2020			
(in thousands, except per share data)	Q1	Q2	Q3	Q4
Operating expenses	$ 72,907	$ 57,175	$ 72,269	$ 49,049
Net loss	$ (74,114)	$ (58,170)	$ (77,665)	$ (54,842)
Net loss per share, basic and diluted	$ (1.49)	$ (1.16)	$ (1.55)	$ (1.09)

(in thousands, except per share data)	2019 Q1	Q2	Q3	Q4
Operating expenses	$ 37,775	$ 37,837	$ 45,096	$ 58,116
Net loss	$ (37,897)	$ (36,626)	$ (44,119)	$ (58,171)
Net loss per share, basic and diluted	$ (0.90)	$ (0.75)	$ (0.89)	$ (1.17)

NOTE 14. SUBSEQUENT EVENTS

On January 6, 2021, the Company and Hercules entered into the sixth amendment to the Term Loan. The sixth amendment provides for, among other things, a decrease in the amount available under the Term Loan from $200.0 million to $75.0 million. The loan repayment schedule provides for interest only payments until April 1, 2022, followed by consecutive equal monthly amortization payments of principal and interest through the maturity date. The maturity date of the Loan Agreement is October 1, 2023, subject to extension to April 1, 2024 on the condition that the Company obtains final approval from the FDA for the NDA for veverimer on or before October 1, 2023. The sixth amendment also eliminates prepayment charges for prepayments of principal of the Term Loan made on or after March 1, 2021. The Company is currently evaluating the accounting for the sixth amendment to the Term Loan.

On January 6, 2021, a putative securities class action was filed in the U.S. District Court for the Northern District of California against Tricida, Inc. and its CEO and CFO, or (the “Securities Class Action”). Pardi v. Tricida, Inc., et al., 21-cv-00076. The Securities Class Action complaint alleges that during the period September 4, 2019 through October 28, 2020 (the “Class Period”), the Company and its senior officers violated the federal securities laws, including under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder, through alleged public misrepresentations and/or omissions of material facts concerning the Company’s NDA for veverimer and the likelihood and timing of approval of veverimer by the FDA. No damages amount is specified in the Securities Class Action.

On February 15, 2021, a derivative action was filed in the District of Delaware, brought by and on behalf of Tricida, Inc. as a Nominal Defendant, against the Company’s directors as well as its CEO and CFO (the “Derivative Case”). Ricks v. Alpern et al., Case No, 1:21-cv-000205. The Derivative Case is based on the allegations of the Securities Class Action and asserts that by allowing the Company and senior executives to make the allegedly false and misleading statements at issue in the Securities Class Action, the defendants breached their fiduciary duties and wasted corporate assets. Additionally, the complaint asserts claims against the senior officers for violation of Sections 10(b) and 21D of the Securities Exchange Act of 1934. No damages amount is specified in the Derivative Case.

In February 2021, the Company received an Appeal Denied Letter, or ADL, from the Office of New Drugs, or OND, of the FDA, in response to its Formal Dispute Resolution Request submitted in December 2020.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

The Company maintains disclosure controls and procedures that are designed to ensure that information required to be disclosed in the Company's reports under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to management, including the Company's Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

The Company's management carried out an evaluation, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures, as defined in Rules 13a–15(e) and 15d–15(e) of the Exchange Act, as of December 31, 2020. Based on the evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that the Company's disclosure controls and procedures were effective as of December 31, 2020.

Management's Annual Report on Internal Control Over Financial Reporting

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a–15(f) and 15d–15(f) under the Exchange Act. The Company's internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. The Company's internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of our Chief Executive Officer and Chief Financial Officer, our management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2020. In making this assessment, management used the criteria set forth in Internal Control—Integrated Framework (2013 framework) issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on this assessment, our management has concluded that the Company's internal control over financial reporting was effective as of December 31, 2020.

Our independent registered public accounting firm, Ernst & Young LLP, has audited our financial statements included in Item 8 of this Annual Report on Form 10-K and have issued a report on our internal control over financial reporting as of December 31, 2020. Their report on the audit of internal control over financial reporting appears below.

Changes in Internal Control over Financial Reporting

There have been no changes to our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the year ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Tricida, Inc.:

Opinion on Internal Control Over Financial Reporting

We have audited Tricida, Inc.'s internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Tricida, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2020 financial statements of the Company and our report dated February 26, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's 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 for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Redwood City, California

February 26, 2021

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

EXECUTIVE OFFICERS AND DIRECTORS

The following table sets forth information regarding our executive officers and directors, as of December 31, 2020.

Name	Age	Position(s)
Executive Officers		
Gerrit Klaerner, Ph.D.	50	President and Chief Executive Officer, Director
Geoffrey M. Parker	56	Executive Vice President and Chief Financial Officer
Dawn Parsell, Ph.D.	58	Executive Vice President of Clinical Development
Robert McKague, Esq.	57	Executive Vice President, General Counsel and Chief Compliance Officer
Wilhelm Stahl, Ph.D.	61	Executive Vice President, Chief Technical Officer
Non-Employee Directors		
Klaus Veitinger, M.D., Ph.D., M.B.A.(1)	58	Chairman of the Board
Robert J. Alpern, M.D.(1)	70	Director
David Bonita, M.D.(1)(2)(3)	45	Director
Sandra I. Coufal, M.D.(2)	57	Director
Kathryn Falberg (3)	60	Director
David Hirsch, M.D., Ph.D.(2)(3)	50	Director

(1) Member of the nominating and corporate governance committee.
(2) Member of the compensation committee.
(3) Member of the audit committee.

Executive Officers

Dr. Gerrit Klaerner, Ph.D., our founder, has served as a member of our board of directors since July 2013 and as our Chief Executive Officer and President since August 2013. Dr. Klaerner was a founder of Relypsa, Inc. and served as its President and as a member of its board of directors from October 2007 until June 2013. Dr. Klaerner co-founded Ilypsa, Inc. in 2003 and served as its Chief Business Officer and Senior Vice President from December 2006 until July 2007 and its Director of Technology Assessment and Business Development from January 2003 until December 2006. Dr. Klaerner served in Symyx Technologies, Inc. from October 1998 until January 2003 as Staff Scientist, Senior Staff Scientist and Director of Business Development. Dr. Klaerner received his Ph.D. in polymer and organic chemistry from the Max Planck Institute for Polymer Research in Mainz, Germany, his M.S. in Chemistry from the Philipps University of Marburg and completed post-doctoral research at Stanford University and the IBM Almaden Research Center.

We believe that Dr. Klaerner is qualified to serve as our President and Chief Executive Officer and on our board of directors because of his extensive experience in leadership and management roles at various life sciences companies.

Mr. Geoffrey M. Parker has served as our Chief Financial Officer and Executive Vice President since April 2017. Mr. Parker previously served as Chief Financial Officer of Anacor Pharmaceuticals, Inc. from September 2010 to May 2015. From 1997 to 2009, Mr. Parker led the West Coast Healthcare Investment Banking practice at Goldman Sachs. Mr. Parker has served as a member of the board of directors of Perrigo Company plc and ChemoCentryx, Inc. since November 2016 and December 2009, respectively. Mr. Parker was also a member of the board of directors of Sunesis Pharmaceuticals, Inc. from March 2016 until December 2017 and Genomic Health, Inc. from June 2016 to November 2019. Mr. Parker holds an AB degree in Economics and Engineering Sciences from Dartmouth College and an M.B.A. from Stanford University.

Dr. Dawn Parsell, Ph.D., has served as our Executive Vice President of Clinical Development since August 2018. Dr. Parsell has over 24 years of biotechnology and pharmaceutical industry experience, where she has been involved in the successful development and approval of nine FDA-approved drugs. She has served as an independent regulatory consultant to the industry since 2001, providing strategic and tactical clinical and regulatory support to her clients, including assisting in the design and implementation of our TRC101 development program since 2014. From 1994 to 2001, Dr. Parsell worked at Connetics Corporation in discovery, clinical development and regulatory affairs positions, most recently as Director of Regulatory Affairs. Dr. Parsell received a B.S. in Biochemistry and Genetics/Cell Biology with Distinction from the University of Minnesota, a Ph.D. in Biology from the Massachusetts Institute of Technology and completed a post-doctoral research fellowship at the Howard Hughes Medical Institute at The University of Chicago.

Mr. Robert McKague, Esq., has served as our Executive Vice President, General Counsel and Chief Compliance Officer since March 2020. Mr. McKague previously worked for over ten years at Jazz Pharmaceuticals where he most recently served as Senior Vice President, Associate General Counsel. At Jazz, he was a member of the Executive Committee and managed a team that supported the global operational functions of the business, including support for six product launches, and ensured compliance with applicable laws, regulations and industry codes of practice in numerous countries. Between 2009 and 2011, Mr. McKague held senior legal positions at Actelion Pharmaceuticals and Oracle America. Mr. McKague began his legal career at the Board of Governors of the Federal Reserve System and Morrison & Foerster, LLP. Mr. McKague received his Juris Doctor from the University of California Hastings College of Law and his Bachelor of Arts in International Relations and French from San Francisco State University.

Dr. Wilhelm Stahl, Ph.D., has served as our Executive Vice President and Chief Technical Officer since February 2017. Dr. Stahl served in a number of roles, including as Senior Vice President of Pharmaceutical Operations and as Chief Technology Officer, at Relypsa, Inc. from September 2011 until January 2017. Since January 2009, Dr. Stahl has been Managing Director of Rondaxe Deutschland OHG, a subsidiary of Rondaxe Enterprises, LLC, a consulting firm, providing consulting services and strategic advice on CMC aspects of drug development, supply chain management and strategic business support, where he was a Managing Partner from October 2009 to September 2011. From 2005 to 2008, Dr. Stahl was Head of the Pharma Custom Manufacturing business of Saltigo GmbH, a subsidiary of Lanxess AG. He received a Ph.D. in Chemistry from the Institute for Organic Chemistry and Biochemistry at the University of Bonn.

Non-Employee Directors

Dr. Klaus R. Veitinger, M.D., Ph.D., M.B.A., has served as a member of our board of directors since February 2014 and as our Chairman of the Board since September 2015. Dr. Veitinger has served as a Venture Partner with OrbiMed Advisors LLC, an affiliate of one of our principal stockholders, since October 2007. Prior to OrbiMed Advisors, Dr. Veitinger was a Member of the Executive Board of Schwarz Pharma AG and the Chief Executive Officer of Schwarz Pharma, Inc. with responsibility for the U.S. and Asia businesses. Dr. Veitinger has served on the boards of public companies, including Intercept Pharmaceuticals, Inc. from August 2012 until July 2016 and Relypsa, Inc. from October 2010 until June 2015, and currently serves on the board of scPharmaceuticals, Inc. since November 2017. Dr. Veitinger currently serves on the boards of directors of the following private companies: Neurogastrx, Inc. and Promentis Pharmaceuticals, Inc. For seven years he was a Director of PhRMA. Dr. Veitinger received his M.D. and his Ph.D. from the University of Heidelberg. He earned his M.B.A. at INSEAD in France.

We believe that Dr. Veitinger is qualified to serve on our board of directors due to his management and investment experience in the life sciences sector and medical and scientific background.

Dr. Robert J. Alpern, M.D., has served as a member of our board of directors since October 2013 and as chairman of our Scientific Advisory Board from October 2013 through May 2018. Dr. Alpern has served as the Ensign Professor of Medicine (Nephrology), and Professor of Internal Medicine at Yale University and as Dean of Yale School of Medicine from June 2004 until January 2020. Dr. Alpern has served as Ensign Professor of Medicine (Nephrology) and Cellular and Molecular Physiology, and as Professor of Internal Medicine and Cellular and Molecular Physiology since February 2020. He served as a Member of the Scientific Advisory Board at Relypsa, Inc. from 2007 until 2014 and Ilypsa, Inc. from 2004 until 2007. From July 1998 until May 2004, Dr. Alpern was the Dean of The University of Texas Southwestern Medical School. Dr. Alpern has also served as a director of AbbVie Inc. since January 2013, Abbott Laboratories since October 2008 and has served on the board of trustees of Yale-New Haven Hospital from October 2005 until January 2020. Dr. Alpern was on the leadership committee of the American Society of Nephrology and served as its president. Dr. Alpern has held or been awarded field-specific journal editorial board and fellowship positions, leadership positions in advisory councils and associations, and teaching awards. Dr. Alpern received his M.D. from the University of Chicago Pritzker School of Medicine and his B.A. in Chemistry from Northwestern University.

We believe that Dr. Alpern is qualified to serve on our board of directors due to his extensive background in medicine and his experience as a board member in the life sciences industry.

Dr. David Bonita, M.D., has served as a member of our board of directors since January 2014. Dr. Bonita is a member of OrbiMed Advisors LLC, an investment firm. Dr. Bonita currently serves on the boards of directors of Acutus Medical Inc., IMARA Inc., Prelude Therapeutics, Inc., and Repare Therapeutics Inc., as well as several private companies. Dr. Bonita also previously served on the boards of directors of Clementia Pharmaceuticals Inc., Loxo Oncology, Inc., SI-BONE, Inc., and ViewRay Inc. Prior to OrbiMed, Dr. Bonita worked as a corporate finance analyst in the healthcare investment banking groups of Morgan Stanley and UBS. He has published scientific articles in peer-reviewed journals based on signal transduction research performed at Harvard Medical School. He received his B.A. in biology from Harvard University and his joint M.D./M.B.A. from Columbia University

We believe that Dr. Bonita is qualified to serve on our board of directors based on his roles on several public and private boards of directors as well as his extensive experience in investing in healthcare companies.

Dr. Sandra I. Coufal, M.D., has served as a member of our board of directors since July 2013 and as a member of our Scientific Advisory Board since August 2013. Dr. Coufal is a co-founder and has served as a co-manager of Sibling Capital Ventures LLC, an affiliate of one of our principal stockholders, since 2013. Dr. Coufal was a co-founder and a co-manager of Sibling Capital, LLC from 2012 to 2016. For the past 19 years, Dr. Coufal has been the Biomedical Advisor for the Genomics Institute of the Novartis Research Foundation. Dr. Coufal served as the Head of the Division of Internal Medicine at the Torrey Pines site of Scripps Clinic from 1997 until 1999, and was a member of the board of directors of Scripps Green Hospital from 1997 until 1999. Dr. Coufal founded and served on Relypsa, Inc.'s Scientific Advisory Board since 2007 and was a co-founder of Ilypsa's Scientific Advisory Board. Dr. Coufal has served on the boards of directors of BioAesthetics Corporation and SafetySpot Inc. since February 2016 and March 2017, respectively. On a volunteer basis, Dr. Coufal has served on the Advisory Board of the New Orleans BioFund since 2017. She has also served in a volunteer capacity on the Advisory Board of The Vision of Children Foundation since 2017. Dr. Coufal has been a Member of the Advisory Board of the Rancho Santa Fe Women's Fund since 2015, serving as its Advisory Chair from 2016-2018. Dr. Coufal served as Associate Faculty in the Division of Internal Medicine for the University of California, San Diego, unsalaried. She completed an internship and residency in Internal Medicine at the University of Texas Southwestern Medical School at Dallas. Dr. Coufal received her M.D. from the University of Texas Southwestern Medical School at Dallas and received her B.S. in Science Preprofessional Studies from the University of Notre Dame and was designated a Notre Dame Scholar.

We believe that Dr. Coufal is qualified to serve on our board of directors due to her experience as an investor in the life sciences industry and her extensive experience as a practicing physician.

Ms. Kathryn Falberg has served as a member of our board of directors since May 2018. From March 2012 to March 2014, Ms. Falberg served as the Executive Vice President and Chief Financial Officer of Jazz Pharmaceuticals plc. From December 2009 to March 2012, Ms. Falberg held the position of Senior Vice President and Chief Financial Officer of Jazz Pharmaceuticals plc. From 2001 through 2009, Ms. Falberg worked with a number of smaller companies while serving as a corporate director and audit committee chair for several companies. From 1995 to 2001, Ms. Falberg served various roles at Amgen Inc., including as Senior Vice President, Finance and Strategy, and Chief Financial Officer, and as Vice President, Chief Accounting Officer, and as Vice President, Treasurer. Ms. Falberg currently serves on the boards of public companies, including Arcus Biosciences, Inc., Nuvation Bio, Urogen Pharma Ltd., and The Trade Desk, Inc. Ms. Falberg previously served on the boards of directors of Aimmune Therapeutics, Axovant Sciences, Ltd., BioMarin Pharmaceutical Inc., Medivation Inc., Halozyme Therapeutics, Inc., aTyr Pharma, Inc., and multiple other companies. Ms. Falberg is an inactive certified public accountant. Ms. Falberg holds an M.B.A. in Finance and B.A. in Economics from the University of California, Los Angeles.

We believe Ms. Falberg is qualified to serve on our board of directors due to her extensive background in the life science industry and her leadership experience as a senior financial executive, director and audit committee member of various other companies in the life science industry.

Dr. David Hirsch, M.D., Ph.D., has served as a member of our board of directors since July 2016. Since 2007, Dr. Hirsch has served as a Founder and Managing Director at Longitude Capital Management, an affiliate of one of our principal stockholders, where he focuses on investments in biotechnology. From 2005 to 2006, Dr. Hirsch was

Vice President of Pequot Ventures where he worked in the life sciences practice. Prior to Pequot Ventures, Dr. Hirsch was an Engagement Manager in the pharmaceutical practice of McKinsey & Co. Dr. Hirsch currently serves on the boards of directors of the following public companies: Molecular Templates, Inc., since 2017 and Poseida Therapeutics, Inc. since 2018. Dr. Hirsch also serves on the boards of directors of the following private companies: Amunix Pharmaceuticals and Rapid Micro Biosystems, Inc., and Dr. Hirsch previously served on the boards of directors of Inflazome, Ltd., Collegium Pharmaceutical, Inc., Civitas Therapeutics, Inc., Precision Therapeutics, Inc., Velicept Therapeutics, Inc., and Zavante Therapeutics, Inc. (acquired by Nabriva (NBVA)). Dr. Hirsch received his B.A. in Biology from The Johns Hopkins University, his M.D. from Harvard Medical School and his Ph.D. in Biology from the Massachusetts Institute of Technology.

We believe that Dr. Hirsch is qualified to serve on our board of directors due to his perspective and experience as an investor and board member in the life sciences industry, as well as his strong medical and scientific background.

CORPORATE GOVERNANCE

Director Independence

Nasdaq rules require that independent directors comprise a majority of a listed company's board of directors. In addition, Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and corporate governance and nominating committees be independent. Our board of directors has determined that Dr. Klaus Veitinger, Dr. Robert Alpern, Dr. David Bonita, Dr. Sandra Coufal, Ms. Kathryn Falberg and Dr. David Hirsch qualify as "independent" directors in accordance with the Nasdaq listing requirements. Dr. Gerrit Klaerner is not independent due to his role as Chief Executive Officer and President of the Company. The Nasdaq independence definition includes a series of objective tests, such as that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by Nasdaq rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Leadership Structure of the Board of Directors

Our amended and restated bylaws and corporate governance guidelines provide our board of directors with flexibility to combine or separate the positions of Chairman of the Board and Chief Executive Officer and/or the implementation of a lead director in accordance with its determination that utilizing one or the other structure would be in the best interests of our Company. Dr. Klaus Veitinger currently serves as our Chairman of the Board.

As a general policy, our board of directors believes that separation of the positions of Chairman of the Board and Chief Executive Officer reinforces the independence of our board of directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of our board of directors as a whole. As such, Dr. Gerrit Klaerner serves as our Chief Executive Officer and President while Dr. Klaus Veitinger serves as our Chairman of the Board but is not an officer of our Company. Our board of directors has concluded that our current leadership structure is appropriate at this time. However, our board of directors continues to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Board of Directors' Role in Risk Oversight

Our board of directors takes an enterprise-wide approach to risk management that seeks to complement our organizational objectives, strategic objectives, long-term organizational performance and the overall enhancement of stockholder value. Our board of directors assesses and considers the risks we face on an ongoing basis, including risks that are associated with our financial position, our competitive position and the impact of our operations on our cost structure. In addition, our board of directors reviews and assesses information regarding cybersecurity risks with management, including regular cybersecurity updates on cyber-attacks; Company-wide cyber awareness training targeting 12 training modules annually and internal phish testing, the results of which are generally reported to the audit committee; and an annual cybersecurity audit including internal and external penetration testing performed by a third-party in the fourth-quarter of each year. Our board of directors' approach to risk management includes understanding the risks we face, analyzing them with the latest information available and determining the steps that should be taken to manage those risks, with a view toward the appropriate level of risk for a company of our size and financial condition.

Certain committees of our board of directors actively manage risk within their given purview and authority. Our audit committee has the responsibility for overseeing our major financial, legal, and regulatory risk exposures, which span a variety of areas including litigation, regulatory compliance, reputational and policy matters, financial reporting and cybersecurity. Our audit committee also oversees the steps our management has taken to monitor and control these exposures, including policies and procedures for assessing and managing risk and related compliance efforts. Our compensation committee evaluates risks arising from compensation policies and practices. Our nominating and corporate governance committee evaluates risks arising from our corporate governance practices. Each of our committees provides reports to the full board of directors regarding these and other matters.

Evaluations of the Board of Directors

The board of directors evaluates its performance and the performance of its committees and individual directors on an annual basis through an evaluation process administered by the nominating and corporate governance committee. The board of directors discusses each evaluation to determine what, if any, actions should be taken to improve the effectiveness of the board of directors or any committee thereof or of the directors.

Meetings of the Board of Directors

Our board of directors held 9 meetings during the year ended December 31, 2020. During 2020, each person currently serving as a director attended at least 80% of the aggregate of the total number of meetings of the board of directors and each committee of which he or she was a member. Each director is also encouraged and expected to attend the Company's annual meeting. All of our directors attended the 2020 annual meeting of stockholders.

Committees of the Board of Directors

Our board of directors has established three standing committees: audit committee, compensation committee and nominating and corporate governance committee. Each committee operates pursuant to a written charter that has been approved by our board of directors. A copy of the current charter for each of the audit committee, compensation committee and nominating and corporate governance committee is available on our website at www.tricida.com by selecting the "Investors" link and then the "Governance" link. The audit committee met 4 times in 2020, the compensation committee met 5 times in 2020 and the nominating and corporate governance committee met once in 2020.

Committee Composition

	Audit Committee	Compensation Committee	Nominating and Governance Committee
Robert J. Alpern, MD			Member
David Bonita, MD	Member	Chairperson	Member
Sandra I. Coufal, MD		Member	
Katherine Falberg (Financial Expert)	Chairperson		
David Hirsch, MD, PhD	Member	Member	
Klaus Veitinger, MD, PhD			Chairperson

= Chairperson = Member = Financial Expert

Audit Committee

Our board of directors has an audit committee and our board of directors has adopted an audit committee charter, which defines the audit committee's principal functions, including oversight related to:

- our accounting and financial reporting process;
- appointing our independent registered public accounting firm;
- evaluating the independent registered public accounting firm's qualifications, independence and performance;
- the compensation, retention, oversight of the work of, and termination of the independent public accounting firm;
- discussing with management and the independent registered public accounting firm the results of the annual audit and the preview of our quarterly financial statements;
- pre-approving all audit and permitted non-audit and tax services to be provided.
- monitoring the rotation of partners of the independent registered public accounting firm on our engagement team in accordance with requirements established by the SEC;
- reviewing our financial statements and our management's discussion and analysis of financial condition and results of operations to be included in our annual and quarterly reports to be filed with the SEC;
- overseeing our risk assessment and risk management process with respect to financial reporting, trading in our securities, fraud healthcare compliance, privacy and cyber-security; and
- reviewing our critical accounting policies and estimates.

All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and Nasdaq. Our board of directors has determined that Ms. Falberg is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable rules and regulations of Nasdaq. Under the rules of the SEC and Nasdaq, members of the audit committee must also meet heightened independence standards. Our board of directors has determined that each of Dr. Bonita, Dr. Hirsch and Ms. Falberg are independent under these heightened audit committee independence standards. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq.

Compensation Committee

Our board of directors has a compensation committee and our board of directors has adopted a compensation committee charter, which defines the compensation committee's principal functions, including recommending policies relating to compensation and benefits of our directors, officers and employees. Among other matters, the compensation committee reviews and approves corporate goals and objectives relevant to compensation of our Chief Executive Officer, evaluate the performance of our Chief Executive Officer in light of those goals and objectives and approves the compensation of the Chief Executive Officer based on such evaluations. The compensation committee also recommends to our board of directors the issuance of stock options and other awards under our stock plans. Each of the members of our compensation committee has been determined to be independent under the applicable rules and regulations of Nasdaq, after considering the additional factors relevant to the independence of compensation committee members under the applicable standards of the SEC and Nasdaq, and is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act. The compensation committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq. The compensation committee may form and delegate authority to subcommittees consisting of one or more members when it deems appropriate.

Nominating and Corporate Governance Committee

Our board of directors has a nominating and corporate governance committee and our board of directors has adopted a nominating and corporate governance committee charter. The nominating and corporate governance committee is responsible for making recommendations to our board of directors regarding candidates for directorships and the size and composition of our board of directors and any of its committees. Among other matters, the nominating and corporate governance committee is responsible for developing and monitoring compliance with our corporate governance guidelines and reporting and making recommendations to our board of directors concerning governance matters. The nominating and corporate governance committee oversees the annual board evaluation process. Each of the members of our nominating and corporate governance committee is an independent director under the applicable rules and regulations of Nasdaq relating to nominating and corporate governance committee independence. The nominating and corporate governance committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq.

In the process of identifying, screening and recommending director candidates to the full board of directors, the nominating and corporate governance committee takes into consideration the needs of the board of directors and the qualifications of the candidates, such as general understanding of various business disciplines (e.g., marketing, finance, etc.), the Company's business environment, educational and professional background, analytical ability, independence, diversity of experience and viewpoints, and willingness to devote adequate time to board of directors duties. The board of directors evaluates each individual in the context of the board of directors as a whole with the objective of retaining a group that is best equipped to help ensure that the long-term interests of the stockholders are served. While the Company does not have a formal policy on diversity for members of the board of directors, the nominating and corporate governance committee values the need for diversity of director skills and viewpoints when considering new candidates. The nominating and corporate governance committee will consider director candidates recommended by stockholders on the same basis that it evaluates other nominees for director.

Compensation Committee Interlocks and Insider Participation

During the year ended December 31, 2020, none of the members of our compensation committee has, at any time, been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee (or other board of directors committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) of any entity that has one or more executive officers on our board of directors or compensation committee.

Corporate Governance Guidelines

The board of directors has adopted our Corporate Governance Guidelines which provide the framework for our corporate governance along with our amended and restated certificate of incorporation, amended and restated bylaws, committee charters and other key governance practices and policies. Our Corporate Governance Guidelines cover a wide range of subjects, including the conduct of board meetings, independence and selection of directors, board membership criteria, and board committee composition. The Corporate Governance Guidelines are available on our website at www.tricida.com by selecting the "Investors" link and then the "Governance" link.

Code of Business Conduct and Ethics

The board of directors has adopted our Code of Business Conduct and Ethics which applies to all of our employees, officers and directors, including those officers responsible for financial reporting. The Code of Business Conduct and Ethics is available on our website at www.tricida.com by selecting the "Investors" link and then the "Governance" link. Any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

Stock Ownership by Directors

The board of directors believes that an ownership stake in the Company strengthens the alignment of interests between directors and stockholders. Accordingly, each director is required to own common stock (or equivalents) having a value of at least three times the annual retainer fee, within three years of becoming a director. In the event the annual retainer fee is increased, directors will have one year to meet the new ownership guidelines. The board of directors will evaluate whether exceptions should be made for any director on whom these guidelines would impose a financial hardship. All of the directors currently comply with these guidelines.

Prohibition on Hedging and Pledging of Company Securities

The Company has a policy that prohibits officers, directors and employees from engaging in hedging transactions, such as the purchase or sale of puts or calls, or the use of any other derivative instruments. Officers, directors and employees of the Company are also prohibited from holding Company securities in a margin account or pledging Company securities as collateral for a loan.

Stockholder Communications

Any stockholder or other interested party who wishes to communicate with our board of directors or any individual director may send written communications to our board of directors or such director c/o Corporate Secretary, Tricida, Inc., 7000 Shoreline Court, Suite 201, South San Francisco, CA 94080. The communication must include the stockholder's name, address and an indication that the person is our stockholder. The Corporate Secretary will review any communications received from stockholders and will forward such communications to the appropriate director or directors, or committee of our board of directors, based on the subject matter.

Delinquent Section 16(a) Reports

Pursuant to Section 16 of the Securities Exchange Act of 1934, executive officers, directors, and holders of more than 10% of the Company's common stock are required to file reports of their trading in Company equity securities with the SEC. Based solely on a review of the copies of such reports received by the Company, or written representations from certain reporting persons, the Company believes that all filings required to be made by its reporting persons complied with all applicable Section 16 filing requirements during the last fiscal year with one exception: a Form 4 reporting a December 11, 2020 acquisition of common stock by Robert McKague was filed on December 23, 2020.

ITEM 11. EXECUTIVE COMPENSATION

Compensation Committee Report

The following report of the compensation committee shall not be deemed to be "soliciting material" or to otherwise be considered "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933, as amended, or the Securities Act, or the Securities Exchange Act of 1934, as amended, or the Exchange Act, except to the extent that the Company specifically incorporates it by reference into such filing.

Our compensation committee has reviewed and discussed the section entitled "Compensation Discussion and Analysis" with our management. Based upon this review and discussion, the compensation committee recommended to the board of directors that the section entitled "Compensation Discussion and Analysis" be included in this Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

Respectfully submitted by the compensation committee of the board of directors.

Dr. David Bonita, M.D., Chair
Dr. Sandra I. Coufal, M.D.
Dr. David Hirsch, M.D., Ph.D.

Compensation Discussion and Analysis

This Compensation Discussion and Analysis contains "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Forward-looking statements relate to expectations concerning matters that are not historical facts. Words such as "projects," "believes," "anticipates," "plans," "expects," "intends," "may," "will," "could," "should," "would," and similar words and expressions are intended to identify forward-looking statements. These forward-looking statements include, but are not limited to, statements related to risks associated with our compensation programs. Readers are cautioned that these forward-looking statements are based on current expectation and are subject to risks, uncertainties, and assumptions that are difficult to predict. We undertake no obligation to revise or update any forward-looking statements for any reason.

This Compensation Discussion and Analysis provides an overview of our executive compensation program for 2020 and our executive compensation philosophies and objectives.

Our named executive officers consist of our Chief Executive Officer, our Chief Financial Officer, our three other most highly compensated executive officers serving in such roles as of December 31, 2020 and one former executive officer of the Company who separated from the Company during 2020 (collectively, the "Named Executive Officers"). For 2020, our Named Executive Officers were:

Name	Title
Gerrit Klaerner, Ph.D.	President and Chief Executive Officer
Geoffrey M. Parker	Executive Vice President, Chief Financial Officer
Dawn Parsell, Ph.D.	Executive Vice President, Clinical Development
Robert McKague	Executive Vice President, General Counsel & Chief Compliance Officer
Wilhelm Stahl, Ph.D.	Executive Vice President, Chief Technology Officer
Susannah Cantrell, Ph.D.(1)	Former Executive Vice President, Chief Commercial Officer

(1) Dr. Cantrell's employment with the Company terminated as of October 30, 2020.

Executive Summary

Our current executive compensation program is intended to align executive compensation with our business objectives and to enable us to attract, retain and reward executive officers who contribute to our long-term success. We seek to accomplish this goal in a way that is aligned with the long-term interests of our stockholders. Our strategy has been to design the Company's compensation programs to drive alignment of all employees, including our Named Executive Officers. We believe that this approach recognizes that, as a Company, we are all one team with one mission. We believe our executive compensation program effectively aligns the interests of our Named Executive Officers with our objective of creating sustainable long-term value for our stockholders.

2020 Highlights

During 2020, our strategic priorities were impacted by the COVID-19 pandemic and the FDA's decision to issue a Complete Response Letter, or CRL, for the New Drug Application, or NDA, for our sole drug product candidate, veverimer, which resulted in a delay in expected approval and commercialization. As such, we were unable to fully execute on our strategic priorities. However, we believe that we have made significant progress on several fronts. Highlights from 2020 include:

- Following the receipt of the CRL, we have made progress with the FDA to understand the deficiencies identified in the CRL and issues identified in the ADL and determine a possible path forward for the resubmission of the NDA for veverimer;
- We laid a strong foundation for the commercial launch of veverimer through an expanded disease education and awareness program, sponsorship of Continuing Medical Education, or CME, programs and over 20 presentations or publications of new data on veverimer, metabolic acidosis, health and economic impacts of metabolic acidosis or the link between metabolic acidosis and CKD progression, and met with 126 payers representing approximately 310 million lives;
- As of December 31, 2020, the VALOR-CKD trial had randomized 1,363 of 1,600 subjects with an average treatment duration of approximately one year and has accrued 57 of the 511 required subjects with positively adjudicated primary endpoint events;
- Continued execution on our global IP strategy, resulting in the allowance of a U.S. patent application that, upon issuance in 2021 will extend protection for veverimer to 2038 in the U.S., and the issuance of an additional 126 patents in 47 different countries, including Australia, China, Israel, Japan, Russia and numerous European and European extension states; and
- In order to secure additional capital to fund operations, in May 2020, we issued $200.0 million aggregate principal amount of 3.50% convertible senior notes due 2027, or Convertible Senior Notes, pursuant to which we pay interest semiannually in arrears at a rate of 3.50% per year.

Due to the delay in regulatory approval and commercialization of veverimer, on September 10, 2020, the compensation committee of the board of directors, or Committee, approved the Tricida, Inc. 2020 Reduction in Force Severance Benefit Plan, or 2020 Restructuring Plan. On September 18, 2020, the Company implemented a restructuring under the 2020 Restructuring Plan to streamline the organization and preserve capital that included the elimination of approximately 21.5% of the Company's workforce and other cost reductions. Following the completion of the Company's Type A meeting with the FDA, on October 25, 2020, the Company's Board of Directors approved and on October 28, 2020, the Company implemented a restructuring under the 2020 Restructuring Plan, or Fourth Quarter 2020 Restructuring, to reduce operating costs and better align its workforce with the needs of its business. Under the Fourth Quarter 2020 Restructuring, the Company reduced its workforce by approximately 60.0% and other cost reductions.

The compensation paid or awarded to our executive officers is generally based on the assessment of each individual's performance compared against the business objectives established for the fiscal year as well as our historical compensation practices. In the case of new hire executive officers, their compensation is primarily determined based on the negotiations of the parties as well as our historical compensation practices. In setting compensation, the Committee also considers the competitive market, as discussed further below, and seeks to recognize and reward high performers through meaningful merit adjustments and bonus and equity incentive opportunities. As in prior years, for 2020, the material elements of our executive compensation program were base salary, a cash incentive opportunity and equity-based compensation in the form of stock options. In addition, in September 2020, the Committee approved a retention program in order to motivate employees and to minimize employee departures during the critical 2020 - 2021 time period for achieving resubmission and approval of the Company's NDA for veverimer and commercial launch. Each continuing employee of the Company, including the Named Executive Officers, participated in the retention program. The retention program applicable to the Named Executive Officers was delivered in the form of performance-based stock options, performance-based cash awards and time-based restricted stock units, or RSUs.

Our Executive Compensation Practices

The Committee reviews on an ongoing basis the Company's executive compensation program to evaluate whether it supports the Company's executive compensation objectives and is aligned with stockholder interests. Our executive compensation practices include the following, each of which the Committee believes reinforces our executive compensation objectives:

- A significant percentage of target annual compensation delivered in the form of variable compensation tied to performance and/or stock price appreciation.
- Our Committee performs a market comparison of executive compensation against a relevant peer group.
- Our Committee retains an independent compensation consultant reporting directly to the Committee and providing no other services to the Company.
- We do not have tax gross-ups for compensation received in connection with a change in control.
- We do not have executive perquisites.
- We do not have excessive severance benefits.
- We do not allow repricing of underwater stock options under our current equity incentive plan without stockholder approval.

2020 Say-On-Pay Vote

The Company received approximately 99.7% support for its "say on pay" vote at the Company's 2020 annual meeting of stockholders. After considering these results, the Committee determined that the Company's executive compensation philosophy, compensation objectives, and compensation elements continued to be appropriate and did not make any specific changes to the Company's executive compensation program in response to the 2020 "say on pay" vote.

Compensation of Named Executive Officers

Base Salary

Base salaries are intended to provide a level of compensation sufficient to attract and retain an effective management team, when considered in combination with the other components of our executive compensation program. The relative levels of base salary for our Named Executive Officers are designed to reflect each executive officer's scope of responsibility and accountability with us. In 2020, the Committee adjusted annual base salary levels based on a review of market data and individual performance. Mr. McKague's base salary was determined when he joined the Company based on a review of market data as well as the Company's historical compensation practices.

The table below sets forth the 2019 and 2020 base salary level for each of our Named Executive Officers:

Named Executive Officer	2019 Annualized Base Salary	2020 Annualized Base Salary
Gerrit Klaerner, Ph.D.	$587,600	$600,000
Geoffrey M. Parker	427,232	437,912
Dawn Parsell, Ph.D.	420,000	436,800
Robert McKague	N/A(1)	400,000
Wilhelm Stahl, Ph.D.	417,768	417,768
Susannah Cantrell, Ph.D.(2)	400,000	418,000

(1) Mr. McKague joined the Company in March 2020. The amount reported for 2020 reflects his annualized base salary and has not been adjusted to reflect his partial year of service.

(2) Dr. Cantrell's employment with the Company terminated in October 2020. The amount reported for 2020 reflects her annualized base salary and has not been adjusted to reflect her partial year of service.

Cash Incentives

During 2020, we provided our senior leadership team with short-term incentive compensation through our cash bonus plan, the Tricida, Inc. Annual Incentive Plan, or the AIP. Cash incentives hold executives accountable, rewards the executives based on actual business results and helps create a "pay for performance" culture. Our AIP provides cash incentive award opportunities for the achievement of performance goals established by the Committee at the beginning of the fiscal year. Payouts to participants vary based on performance as compared to the target performance goals established by the Committee. The Committee also retains discretion to reduce payouts for any factors it deems appropriate.

The table below sets forth the 2019 and 2020 target bonus opportunities for each of our Named Executive Officers under the AIP:

Named Executive Officer	2019 Target Bonus Opportunities	2020 Target Bonus Opportunities
Gerrit Klaerner, Ph.D.	55%	60%
Geoffrey M. Parker	40%	45%
Dawn Parsell, Ph.D.	30%	40%
Robert McKague(1)	N/A	40%
Wilhelm Stahl, Ph.D.	30%	40%
Susannah Cantrell, Ph.D.(2)	35%	40%

(1) Mr. McKague's target opportunity was determined when he joined the Company in March 2020 based on a review of market data but was increased from 30% to 40% in September 2020 by the Committee retroactively to align with the Company's historical compensation practices.

(2) Dr. Cantrell's employment with the Company terminated in October 2020 and she was therefore ineligible to receive payout under the 2020 AIP.

2020 AIP Pay-for-Performance Alignment

The Committee undertakes a rigorous review and analysis to establish performance goals under the AIP. For each Named Executive Officer other than Dr. Klaerner, 50% of his or her 2020 AIP target was based on a qualitative assessment of individual performance and 50% was based on Company-wide performance goals relating to (i) regulatory developments, (ii) commercial operations, (iii) clinical activities, (iv) technical operations and (v) financial activities. Dr. Klaerner's entire 2020 AIP target was based on Company-wide performance goals. For 2020, the Committee established the following performance goals and weightings under the AIP with respect to the Company-wide performance goals. The performance goals were designed to be achievable, but required the coordinated, cross-functional focus and effort of the executives.

- Regulatory Developments (weighted 30%) - achieve FDA approval for veverimer by the PDUFA date of August 22, 2020

- Commercial Operations (weighted 30%) - achieve successful launch of veverimer
- Clinical Activities (weighted 15%) - complete enrollment in the ongoing VALOR-CKD trial
- Technical Operations (weighted 12.5%) - provide drug product to support commercial launch
- Financial Activities (weighted 12.5%) - to fund operations to profitability

As previously disclosed, in August 2020, the Company received a CRL from the FDA related to the Company's NDA for veverimer. The resulting delay in regulatory approval also impacted the goals associated with commercialization and profitability. The timeline for completion of enrollment of the ongoing VALOR-CKD trial was extended beyond the end of 2020. Accordingly, management recommended and the Committee determined that 2020 AIP would not fund and, accordingly, none of our Named Executive Officers received a payout under the 2020 AIP.

Equity Incentive Program

To further align the interests of our executive officers with the interests of our stockholders and to further focus our executive officers on our long-term performance, we have historically granted equity compensation in the form of stock options. The 2020 equity grants were determined based on individual performance, input of the Committee's independent compensation consultant, and the Committee's review of the public company market data described below, with the general goal of aligning equity compensation with the 75th percentile of the market data. Mr. McKague's grant also consisted of a new hire grant, with the value determined based on the Company's historical compensation practices as well as relevant market data. In early 2020, the Committee awarded Dr. Klaerner, Mr. Parker, Dr. Parsell, Mr. McKague, Dr. Stahl and Dr. Cantrell stock options to purchase 292,000, 130,000, 130,000, 210,000, 40,000 and 100,000 shares of our common stock, respectively. The 2020 stock option grants generally vest 25% on the first anniversary of the vesting commencement date and in subsequent 1/36th increments for each subsequent month of continuous employment.

Retention Awards

In September 2020, the Committee approved performance-based retention awards to the Company's employees, including each of the then-serving Named Executive Officers, which were intended to retain and incent the executive officers and further align their interests with the interests of our stockholders. Specifically, these retention awards were granted to motivate employees and to minimize employee departures during the critical 2020 - 2021 time period for achieving approval of the Company's NDA for veverimer and commercial launch. The retention awards program was designed to reward employee performance and achievement based on the attainment of the following corporate objectives which were deemed critical to the Company's success:

1) Occurrence of the Type A meeting with the FDA by December 31, 2020;

2) Resubmission of the NDA for veverimer by December 31, 2022;

3) Approval of the NDA for veverimer by December 31, 2022; and

4) Commercial launch by December 31, 2022.

The retention award amounts, which consisted of cash and equity components, were determined after consultation with Compensia. The retention awards granted to the Company's Named Executive Officers consisted of (i) stock options, which were equal to one-half the annual stock award value, vest 25% upon an NDA resubmission, 50% upon an NDA approval and 25% upon a commercial launch, in each case, that occurs by December 31, 2022 (the "Retention Stock Options"); (ii) RSUs, which were calculated as a percentage of the then-current 2020 annual base salary, will fully vest on December 31, 2021, subject to the executive's continued employment through the vesting date (the "Retention RSUs"); and (iii) cash retention awards (the "Cash Retention Awards"), which were calculated as a percentage of the then-current 2020 annual base salary, will vest in four equal installments upon the occurrence of each of the corporate objectives described above. A Type A meeting occurred in October 2020 and the first installments of the Cash Retention Awards were accordingly paid in November 2020. In addition, Dr. Klaerner received a grant of 100,000 stock options with vesting subject to NDA approval for veverimer by December 31, 2022.

The table below shows the target number of shares subject to the Retention Stock Options and Retention RSUs and the target amount of the Cash Retention Awards for each Named Executive Officer.

Named Executive Officer	Target Number of Shares Subject to Retention Stock Options	Target Number of Shares Subject to Retention RSUs	Target Cash Retention Award
Gerrit Klaerner, Ph.D.	246,000(1)	8,000	$480,000
Geoffrey M. Parker	65,000	4,000	218,956
Dawn Parsell, Ph.D.	65,000	4,000	218,400
Robert McKague	52,500	4,000	200,000
Wilhelm Stahl, Ph.D.	50,000	4,000	208,884
Susannah Cantrell, Ph.D.(2)	50,000	4,000	209,000

(1) This amount includes the additional stock option grant of 100,000 shares with vesting based on NDA approval for veverimer by December 31, 2022.
(2) Dr. Cantrell forfeited her retention awards upon her departure from the Company in October 2020.

Other Elements of Our 2020 Executive Compensation Program

Severance Arrangements

During 2020, the Named Executive Officers were each participants in the Tricida, Inc. Executive Severance Benefit Plan, as amended, or the Executive Severance Plan, which provides severance benefits upon certain qualifying terminations of employment with the Company. The Committee believes that these severance benefits help secure the continued employment and dedication of our Named Executive Officers and are important as a recruitment and retention device, as many of the companies with which we compete for executive talent have similar arrangements in place for their senior management. The terms of the severance benefits were determined based on a review of market practices and the input of the Committee's independent compensation consultant and, consistent with market practices, do not include change in control-related tax gross-ups.

In February 2020, the Committee amended the Executive Severance Plan to create a new tier of benefits for employees holding the title of Executive Vice President. As a result of the amendment, the cash severance benefits payable to such employees, expressed as a multiple of a participant's monthly base salary, were increased based on a review of market data. Following this amendment, the cash severance benefit, expressed as a multiple of monthly base salary, and the number of months of fully-subsidized COBRA continuation coverage, in each case, were increased (i) from nine months to 10 months for a qualifying termination not in connection with a change in control and (ii) from 12 months to 15 months for a qualifying termination in connection with a change in control. The Named Executive Officers, other than the Chief Executive Officer, are under this new tier of benefits.

In connection with her termination of employment in October 2020, Dr. Cantrell was eligible to receive ten months of cash severance benefits and fully subsidized COBRA continuation coverage, as described above. Pursuant to the terms of the applicable award agreements, Dr. Cantrell forfeited all equity awards held by her that were unvested as of her termination date.

See the "2020 Potential Payments upon Termination or Change in Control" section for additional information regarding the employment arrangements with each of our Named Executive Officers, including a quantification of benefits that would have been received by each Named Executive Officer had his or her employment terminated on December 31, 2020 or, in the case of Dr. Cantrell received upon termination of employment.

Other Benefits

Our Named Executive Officers participate in our corporate-wide benefit programs. Our Named Executive Officers are offered benefits that generally are commensurate with the benefits provided to all of our full-time employee, which includes participation in our qualified defined contribution plan. We do not provide perquisites that are often provided at other companies to executive officers.

How We Make Executive Compensation Decisions

Role of the Board, Compensation Committee and our Executive Officers

The Committee is responsible for determining the compensation of our Chief Executive Officer and each of our other executive officers. In setting the compensation of our Chief Executive Officer, the Committee takes into account the nominating and corporate governance committee's review of the Chief Executive Officer's performance. In setting the compensation of our other executive officers, the Committee takes into account the Chief Executive Officer's review of each executive officer's performance and his recommendations with respect to their compensation. The Committee's responsibilities regarding executive compensation are further described in the "Corporate Governance" section of this Annual Report on Form 10-K.

Guidance from Independent Compensation Consultant

Compensia is engaged at the sole discretion of the Committee to provide executive compensation consulting services. With respect to 2020, Compensia provided services related to the review of 2020 compensation adjustments, including a review of peer group compensation data, awards under our equity incentive program, the setting of performance goals in our annual incentive plan, an analysis of the relationship between the Company's pay and performance relative to peers, trends and tax and regulatory developments with respect to executive compensation, our compensation peer group, our non-employee director compensation program, advised on our 2020 retention awards program and assistance with this Compensation Discussion and Analysis. Compensia is retained by and reports to the Committee and, at the request of the Committee, participates in Committee meetings. Compensia did not provide any services to the Company with respect to 2020 other than those provided to the Committee. The Committee reviewed the independence of Compensia under Nasdaq and SEC rules and concluded that the work of Compensia has not raised any conflict of interest.

Comparison to Relevant Peer Group

To obtain a broad view of competitive practices among industry peers and competitors for executive talent, the Committee reviews market data for peer group companies. The Committee believes that our executive compensation peer group should reflect the markets in which the Company competes for business, executive talent and capital and selects companies based on the following peer selection criteria:

- Industry: Biotechnology & Pharmaceuticals
- Market Capitalization: $560 million to $6.7 billion (approximately 1/3x to 4x the Company's market capitalization)
- Stage of Lead Drug Candidate
- Revenue comparability
- Number of employees
- Therapeutic focus
- Location
- Total Shareholder Return

In selecting companies for our peer group, the Committee considers recommendations from Compensia. The Committee approved the following peer group of companies to evaluate 2020 executive compensation decisions: Acceleron Pharma; Aimmune Therapeutics; Arena Pharmaceuticals; Biohaven Pharmaceutical; Cara Therapeutics; ChemoCentryx; Cytokinetics; Deciphera Pharmaceuticals; Epizyme; Esperion Therapeutics; FibroGen; Global Blood Therapeutics; Iovance Biotherapeutics; Karyopharm Therapeutics; MyoKardia; Reata Pharmaceuticals; Rhythm Pharmaceutical; Xencor; and Zogenix. This is the same peer group that was used for evaluating 2019 compensation decisions, except Alder BioPharmaceuticals was removed due to its acquisition, and ImmunoGen, MacroGenics and Retrophin were removed due to low market capitalization and Cytokinetics, Epizyme, FibroGen and Iovance Biotherapeutics were added in order to better align the Company to industry peers with similar market capitalization.

We believe that the compensation practices of our 2020 peer group provided us with appropriate benchmarks for evaluating the compensation of our Named Executive Officers for 2020 because of the developmental, market and organizational characteristics we shared with the companies in our peer group. In comparing the Company's executive compensation program to the peer group, the Committee generally seeks to align cash compensation with the 50th percentile of the peer group and equity compensation with the 75th percentile of the peer group, with deviations to recognize and reward high performers.

2020 Summary Compensation Table

The following table shows information regarding the compensation of our Named Executive Officers for services performed in the year ended December 31, 2020 and, to the extent required by applicable SEC executive compensation disclosure rules, December 31, 2019 and 2018.

Name and Principal Position	Year	Salary ($)(1)	Bonus ($)(2)	Stock Awards ($)(3)	Option Awards ($)(4)	Non-Equity Incentive Plan Compensation ($)(5)	All Other Compensation ($)(6)	Total ($)
Gerrit Klaerner, Ph.D., President and Chief Executive Officer	2020	$597,933	$0	$93,680	$8,076,824	$120,000	$2,043	$8,890,480
	2019	583,833	64,636	—	9,195,004	323,180	2,043	10,168,696
	2018	503,333	—	—	682,982	310,750	—	1,497,065
Geoffrey M. Parker, Executive Vice President, Chief Financial Officer	2020	436,132	11,464	46,840	3,280,636	54,739	—	3,829,811
	2019	424,493	—	—	2,161,167	196,527	—	2,782,187
	2018	407,508	—	—	147,364	164,320	2,333	721,525
Dawn Parsell, Ph.D., Executive Vice President, Clinical Development	2020	434,000	16,316	46,840	3,280,636	54,600	—	3,832,392
	2019	416,667	17,053	—	2,373,266	144,900	—	2,951,886
	2018	166,667	15,576	—	3,172,187	50,000	253,989	3,658,419
Robert McKague, Executive Vice President, General Counsel & Chief Compliance Officer	2020	325,000	111,464	46,840	4,352,992	50,000	—	4,886,296
Wilhelm Stahl, Ph.D., Executive Vice President, Chief Technology Officer	2020	417,768	—	46,840	1,221,422	52,221	2,073	1,740,324
Susannah Cantrell, Ph.D., Executive Vice President, Chief Commercial Officer	2020	345,333	—	46,840	2,523,566	52,250	381,326	3,349,315
	2019	372,821	100,000	—	3,445,047	150,500	2,153	4,070,521

(1) The amounts reflect the base salaries earned during each reporting year.

(2) The amount reported in this column for Mr. McKague represents (i) a $100,000 sign-on bonus granted in connection with his commencement of employment with us and (ii) a one-time bonus of $11,464. The amounts reported in this column for Mr. Parker and Dr. Parsell represent one-time bonuses of $11,464 and $16,316, respectively.

(3) For 2020, amounts reflect the aggregate grant date fair value of the Retention RSUs granted in 2020, computed in accordance with FASB ASC Topic 718, Compensation-Stock Compensation, based on the closing stock price on the date of grant.

(4) For 2020, amounts reflect the aggregate grant date fair value of stock options awarded in 2020, computed in accordance with FASB ASC Topic 718, Compensation-Stock Compensation based on the following assumptions: risk-free interest rate of 0.3%–1.3%; expected volatility of 68.7%–73.2%; expected term of 5.2–6.1 years and expected dividend rate of 0%. The amounts included in this column for the Retention Stock Options are calculated based on the probable satisfaction of the performance conditions for such awards at the time of grant. Assuming the highest level of performance is achieved for the Retention Stock Options, the maximum value of these awards at the grant date would be as follows: Dr. Klaerner $1,739,723; Mr. Parker $459,324; Dr. Parsell $459,324; Mr. McKague $370,993; Dr. Stahl $353,326; and Dr. Cantrell $353,326.

(5) The amounts represent the first installment of the Cash Retention Awards paid in November 2020 based on the Company achieving the performance criteria relating to the occurrence of a Type A meeting in October 2020. Please see the Compensation Discussion & Analysis for further information regarding the Cash Retention Awards.

(6) All other compensation for the year ended December 31, 2020 represents (i) premiums for life insurance for Dr. Klaerner and Dr. Stahl and (ii) severance benefits that Dr. Cantrell became eligible to receive under the Executive Severance Plan in connection with her termination of employment in October 2020 ($381,326).

2020 Grants of Plan-Based Awards Table

The following table provides information regarding the possible payouts to our Named Executive Officers in 2020 under the AIP, the Cash Retention Awards and the equity awards received by our Named Executive Officers in 2020 under the Tricida, Inc. 2018 Equity Incentive Plan, or the 2018 Plan.

Name	Grant Date	Estimated Possible Payouts Under Non-equity Incentive Plan Awards			Estimated Possible Payouts Under Equity Incentive Plan Awards[1]			All Other Stock Awards: Number of Shares of Stock or Units[2]	All Other Option Awards: Number of Securities Underlying Options (#)[3]	Exercise or Base Price of Option Awards ($)	Grant Date Fair Value of Stock and Option Awards ($)[4]
		Threshold ($)	Target ($)	Maximum ($)	Threshold (#)	Target (#)	Maximum (#)				
Gerrit Klaerner, Ph.D.	—[5]	$—	$360,000	$—	—	—	—	—	—	$—	$—
	—[6]	120,000	480,000	480,000	—	—	—	—	—	—	—
	2/24/2020	—	—	—	—	—	—	—	292,000	35.12	6,337,101
	9/10/2020	—	—	—	36,500	146,000	146,000	—	—	11.71	1,031,713
	9/10/2020	—	—	—	—	100,000	—	—	—	11.71	708,010
	9/10/2020	—	—	—	—	—	—	8,000	—	—	93,680
Geoffrey M. Parker	—[5]	—	197,060	—	—	—	—	—	—	—	—
	—[6]	54,739	218,956	218,956	—	—	—	—	—	—	—
	2/24/2020	—	—	—	—	—	—	—	130,000	35.12	2,821,312
	9/10/2020	—	—	—	16,250	65,000	65,000	—	—	11.71	459,324
	9/10/2020	—	—	—	—	—	—	4,000	—	—	46,840
Dawn Parsell, Ph.D.	—[5]	—	196,560	—	—	—	—	—	—	—	—
	—[6]	54,600	218,400	218,400	—	—	—	—	—	—	—
	2/24/2020	—	—	—	—	—	—	—	130,000	35.12	2,821,312
	9/10/2020	—	—	—	16,250	65,000	65,000	—	—	11.71	459,324
	9/10/2020	—	—	—	—	—	—	4,000	—	—	46,840
Robert McKague	—[5]	—	160,000	—	—	—	—	—	—	—	—
	—[6]	50,000	200,000	200,000	—	—	—	—	—	—	—
	3/9/2020	—	—	—	—	—	—	—	210,000	31.14	3,981,999
	9/10/2020	—	—	—	13,125	52,500	52,500	—	—	11.71	370,993
	9/10/2020	—	—	—	—	—	—	4,000	—	—	46,840
Wilhelm Stahl, Ph.D.	—[5]	—	167,107	—	—	—	—	—	—	—	—
	—[6]	52,221	208,884	208,884	—	—	—	—	—	—	—
	2/24/2020	—	—	—	—	—	—	—	40,000	35.12	868,096
	9/10/2020	—	—	—	12,500	50,000	50,000	—	—	11.71	353,326
	9/10/2020	—	—	—	—	—	—	4,000	—	—	46,840
Susannah Cantrell, Ph.D.	—[5]	—	167,200	—	—	—	—	—	—	—	—
	—[6]	52,250	209,000	209,000	—	—	—	—	—	—	—
	2/24/2020	—	—	—	—	—	—	—	100,000	35.12	2,170,240
	9/10/2020	—	—	—	12,500	50,000	50,000	—	—	11.71	353,326
	9/10/2020	—	—	—	—	—	—	4,000	—	—	46,840

(1) These amounts represent the threshold, target and maximum share amounts of the Retention Stock Options granted under the 2018 Plan, which, for actively employed executives and other than Dr. Klaerner's grant of 100,000 stock options, vest 25% upon an NDA resubmission, 50% upon an NDA approval and 25% upon a commercial launch, in each case, that occurs by December 31, 2022. Dr. Klaerner's grant of 100,000 stock options vest upon NDA approval for veverimer by December 31, 2022.

(2) These amounts represent Retention RSUs granted under the 2018 Plan, which, for actively employed executives, vest 100% on December 31, 2021, subject to the executive's continued employment through the vesting date.

(3) These amounts represent stock options granted under the 2018 Plan. For actively employed executives, the options vest 25% on the first anniversary of the grant date and in subsequent 1/36th increments for each subsequent month of continuous employment.

(4) These amounts reported represent the aggregate grant date fair value of stock options and RSUs awarded in 2020, computed in accordance with FASB ASC Topic 718, Compensation-Stock Compensation. The amounts reported with respect to stock options are based on the following assumptions: risk-free interest rate of 0.3%–1.3%; expected volatility of 68.7%–73.2%; expected term of 5.2–6.1 years and expected dividend rate of 0%. The amounts reported with respect to the Retention Stock Options are based upon the probable outcome of the applicable performance conditions.

(5) These amounts represent target cash award levels set in 2020 under the AIP. As noted in the Compensation Discussion and Analysis, the Company did not pay any bonuses under the AIP for 2020.

(6) The threshold, target and maximum plan award amounts reported in these columns represents 25%, 100% and 100% respectively, of the maximum potential payouts under the Cash Retention Awards. Amounts actually paid to the Named Executive Officer with respect to the Cash Retention Awards in 2020 are reported as Non-Equity Incentive Plan Compensation in the 2020 Summary Compensation Table.

Outstanding Equity Awards at 2020 Fiscal Year-End

The following table presents information regarding the outstanding stock options and RSUs held by each of the named executive officers as of December 31, 2020. Outstanding stock options held by Dr. Cantrell as of December 31, 2020 were canceled in January 2021.

			Option Awards					Stock Awards	
Name	Grant Date	Vesting Commencement Date	Number of Securities Underlying Unexercised Options (#) Exercisable(1)(2)	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)(3)	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)(4)	Market Value of Shares or Units of Stock That Have Not Vested ($)(5)
Gerrit Klaerner Ph.D.	3/9/2015	3/1/2015	109,296	—	—	$ 0.80	3/8/2025	—	$ —
	2/24/2016	1/1/2016	75,376	—	—	0.96	2/23/2026	—	—
	9/27/2016	6/8/2016	76,633	—	—	1.68	9/26/2026	—	—
	11/3/2016	10/1/2016	115,577	—	—	1.68	11/2/2026	—	—
	9/15/2017	9/1/2017	144,472	—	—	2.39	9/14/2027	—	—
	3/15/2018	3/15/2018	125,628	—	—	7.49	3/15/2028	—	—
	5/15/2018	5/15/2018	25,125	—	—	7.89	5/14/2028	—	—
	2/20/2019	2/20/2019	450,000	—	—	22.82	2/19/2029	—	—
	8/22/2019	8/22/2019	110,000	—	—	34.27	8/21/2029	—	—
	2/24/2020	2/24/2020	292,000	—	—	35.12	2/23/2030	—	—
	9/10/2020	9/10/2020	—	—	—	—	—	8,000	56,400
	9/10/2020	9/10/2020	—	—	146,000	11.71	9/9/2030	—	—
	9/10/2020	9/10/2020	—	—	100,000	11.71	9/9/2030	—	—
Geoffrey M. Parker	6/15/2017	4/10/2017	196,909	—	—	1.84	6/14/2027	—	—
	9/15/2017	9/1/2017	30,150	—	—	2.39	9/14/2027	—	—
	3/15/2018	3/15/2018	35,175	—	—	7.49	3/15/2028	—	—
	2/20/2019	2/20/2019	100,000	—	—	22.82	2/19/2029	—	—
	8/22/2019	8/22/2019	30,000	—	—	34.27	8/21/2029	—	—
	2/24/2020	2/24/2020	130,000	—	—	35.12	2/23/2030	—	—
	9/10/2020	9/10/2020	—	—	—	—	—	4,000	28,200
	9/10/2020	9/10/2020	—	—	65,000	11.71	9/9/2030	—	—
Dawn Parsell, Ph.D.	9/27/2016	6/8/2016	420	—	—	1.68	9/26/2026	—	—
	11/3/2016	10/1/2016	4,190	—	—	1.68	11/2/2026	—	—
	9/15/2017	9/1/2017	15,386	—	—	2.39	9/13/2027	—	—
	3/15/2018	3/15/2018	23,033	—	—	7.49	3/15/2028	—	—
	9/27/2018	8/1/2018	125,000	—	—	31.85	9/26/2028	—	—
	2/20/2019	2/20/2019	100,000	—	—	22.82	2/19/2029	—	—
	8/22/2019	8/22/2019	40,000	—	—	34.27	8/21/2029	—	—
	2/24/2020	2/24/2020	130,000	—	—	35.12	2/23/2030	—	—
	9/10/2020	9/10/2020	—	—	—	—	—	4,000	28,200
	9/10/2020	9/10/2020	—	—	65,000	11.71	9/9/2030	—	—
Robert McKague	3/9/2020	3/9/2020	210,000	—	—	31.14	3/8/2030	—	—
	9/10/2020	9/10/2020	—	—	—	—	—	4,000	28,200
	9/10/2020	9/10/2020	—	—	52,500	11.71	9/9/2030	—	—
Wilhelm Stahl, Ph.D.	2/8/2017	2/1/2017	199,942	—	—	1.68	2/7/2027	—	—
	9/15/2017	9/1/2017	30,150	—	—	2.39	46,644.00	—	—
	3/15/2018	3/15/2018	27,638	—	—	7.49	3/15/2028	—	—
	2/20/2019	2/20/2019	60,000	—	—	22.82	2/19/2029	—	—
	8/22/2019	8/22/2019	30,000	—	—	34.27	8/21/2029	—	—
	2/24/2020	2/24/2020	40,000	—	—	35.12	2/23/2030	—	—
	9/10/2020	9/10/2020	—	—	—			4,000	28,200
	9/10/2020	9/10/2020	—	—	50,000	11.71	9/9/2030	—	—

(1) These options vest 25% on the first anniversary of the vesting commencement date and in subsequent 1/48th increments for each subsequent month of continuous employment, except that (i) the options granted on February 20, 2019 and February 24, 2020 vest or vested 25% on the first anniversary of the vesting commencement date and in subsequent 1/36th increments for each subsequent month of continuous employment and (ii) the options granted on August 22, 2019 vest in 18 monthly installments subject to the executive's continued employment.

(2) Because time-based options granted to our Named Executive Officers may be early exercised for restricted stock, options are reported in this table as "Exercisable." Please see footnote (1) to this table for the vesting schedule applicable to the option awards.

(3) Other than Dr. Klaerner's option with respect to 100,000 shares, these options vest 25% upon an NDA resubmission, 50% upon an NDA approval and 25% upon a commercial launch, in each case, that occurs by December 31, 2022. Dr. Klaerner's grant of 100,000 stock options vest upon NDA approval for veverimer by December 31, 2022.
(4) These RSUs vest 100% on December 31, 2021, subject to the executive's continuous employment through the vesting date.
(5) The amounts in this column have been calculated using the December 31, 2020 closing share price of $7.05.

2020 Stock Option Exercises Table

The following table provides information concerning the exercise of stock options during 2020 for each of the Named Executive Officers. None of the RSUs held by the Named Executive Officers vested in 2020.

	Option Awards	
Name	**Number of Shares Acquired on Exercise (#)**	**Value Realized on Exercise ($)**
Gerrit Klaerner Ph.D.	—	$ —
Geoffrey M. Parker	—	—
Dawn Parsell, Ph.D.	21,250	666,118
Robert McKague	—	—
Wilhelm Stahl, Ph.D.	500	18,615
Susannah Cantrell, Ph.D.	—	—

2020 Potential Payments Upon a Termination or Change in Control

Each of our Named Executive Officers participates in the Tricida, Inc. Executive Severance Benefit Plan, as amended, or the Executive Severance Plan. In the event a participant in the Executive Severance Plan experiences a termination without "cause" or resigns for "good reason," each as defined in the Executive Severance Plan, then such participant will be eligible to receive (i) a cash severance benefit in an amount equal to a specified number of months of base salary, payable in monthly installments, and (ii) Company-paid premiums for healthcare continuation coverage during the severance period while the participant continues to participate in our health plans or until the participant is entitled to alternative coverage. The period for monthly severance benefits is equal to 12 months for Dr. Klaerner and ten months for the other Named Executive Officers.

In connection with her termination of employment in October 2020, Dr. Cantrell was eligible to receive ten months of cash severance benefits ($348,333) and fully subsidized COBRA continuation coverage ($32,993) pursuant to the terms of the Executive Severance Plan. Pursuant to the terms of the applicable award agreements, Dr. Cantrell forfeited all equity awards held by her that were unvested as of her termination date.

The following table sets for the termination related benefits that the Named Executive Officers other than Dr. Cantrell would have received in the event of a termination not related to a change in control as of December 31, 2020.

Potential Payments Upon a Qualifying Termination of Employment[(1)]

Name	**Severance Payment ($)[(2)]**	**Welfare Benefits ($)[(3)]**	**Aggregate Payments ($)**
Gerrit Klaerner Ph.D.	$ 600,000	$ 42,060	$ 642,060
Geoffrey M. Parker	364,927	35,050	399,977
Dawn Parsell, Ph.D.	364,000	—	364,000
Robert McKague	333,333	11,104	344,437
Wilhelm Stahl, Ph.D.	348,140	23,429	371,569

(1) A qualifying termination means termination of the Named Executive Officer's employment (1) by the Company other than (A) for "cause," (B) the Named Executive Officer's death or (C) the Named Executive Officer's disability, or (2) by the Named Executive Officer for "good reason."
(2) Amounts reported in this column represent the monthly severance multiple times the Named Executive Officer's monthly base salary. As of December 31, 2020, the monthly severance multiple was 12 for Dr. Klaerner and ten for the other Named Executive Officers.
(3) Represents the estimated value of continued welfare benefits that all Named Executive Officers would be entitled to receive upon a qualifying termination of employment.

In the event an Executive Severance Plan participant's employment is terminated without cause or due to good reason within three months prior to, or 15 months following, a change in control, separation benefits will consist of: (i) monthly severance benefits equal to 18 months for Dr. Klaerner and 15 months for the other Named Executive Officers; (ii) immediate vesting of any outstanding and unvested equity awards; and (iii) an additional cash payment equal to the participant's target annual bonus for the year of termination, prorated based on the number of months in the year prior to the date of termination if, as of the date of the participant's termination of employment, the Company and participant were on "target" to achieve the applicable performance goals.

Potential Payments Upon a Qualifying Termination of Employment Following a Change in Control[(1)]

Name	Severance Payment ($)[(2)]	Target Bonus ($)[(3)]	Value of Accelerated Equity Awards ($)[(4)]	Welfare Benefits ($)[(5)]	Aggregate Payments ($)
Gerrit Klaerner, Ph.D.	$ 900,000	$ 360,000	$ 182,649	$ 42,060	$ 1,484,709
Geoffrey M. Parker	547,390	197,060	163,659	35,050	943,159
Dawn Parsell, Ph.D.	546,000	196,560	50,177	—	792,737
Robert McKague	500,000	160,000	28,200	11,104	699,304
Wilhelm Stahl, Ph.D.	522,210	167,107	103,477	23,429	816,223

(1) A qualifying termination means termination of the Named Executive Officer's employment within three months prior to or 15 months following a change in control (1) by the Company other than (A) for "cause," (B) the Named Executive Officer's death or (C) the Named Executive Officer's disability, or (2) by the Named Executive Officer for "good reason."

(2) Amounts reported in this column represent the monthly severance multiple times the Named Executive Officer's monthly base salary. As of December 31, 2020, the monthly severance multiple was 18 for Dr. Klaerner and 15 for the other Named Executive Officers.

(3) Represents an additional severance benefit equal to the Named Executive Officer's target annual bonus for the year of termination, prorated based on the number of months in the year prior to the date of termination if, as of the date of the participant's termination of employment, the Company and participant were on "target" to achieve the applicable performance goals. Because the termination is deemed to have occurred as of December 31, 2020, the entire target bonus is included.

(4) Under the terms of the Executive Severance Plan, all outstanding equity awards would vest in full. The value of the accelerated vesting of the equity awards reported in this table is based upon our closing stock price of $7.05 on December 31, 2020.

(5) Represents the estimated value of continued welfare benefits that all Named Executive Officers would be entitled to receive upon a qualifying termination of employment.

Risks Related to Compensation Policies and Practices

When determining our compensation policies and practices, the Board considers various matters relevant to the development of a reasonable and prudent compensation program, including whether the policies and practices are reasonably likely to have a material adverse effect on us. We believe that the mix and design of our executive compensation plans and policies do not encourage management to assume excessive risks and are not reasonably likely to have a material adverse effect on us.

CEO Pay Ratio

As required by Section 953(b) of the Dodd-Frank Wall Street Reform and Consumer Protection Act, the Company is providing the following disclosure about the relationship of the annual total compensation of our coworkers to the annual total compensation of Dr. Klaerner, our Chief Executive Officer and President during 2020. SEC rules for identifying the median employee and calculating the pay ratio allow companies to apply various methodologies and assumptions and, as a result, the pay ratio reported by us may not be comparable to the pay ratio reported by other companies. Given the leverage of our executive compensation program towards performance-based elements, we expect that our pay ratio disclosure will fluctuate year-to-year based on the Company's performance against the pre-established performance goals.

Ratio

For 2020,

- The median of the annual total compensation of all of our employees, other than Dr. Klaerner, was $353,567.

- Dr. Klaerner's annual total compensation, as reported in the Total column of the 2020 Summary Compensation Table, was $8,890,480.
- Based on this information, the ratio of the annual total compensation of Dr. Klaerner to the median of the annual total compensation of all employees is estimated to be 25 to 1. We believe this ratio is a reasonable estimate calculated in a manner consistent with Item 402(u) of Regulation S-K.

Identification of Median Employee

We selected December 31, 2020 as the date on which to determine our median employee. For purposes of identifying the median employee from our employee population base of approximately 63 employees, we considered all of our employees, as compiled from our payroll records. We selected actual base salary paid for 2020, actual 2020 bonus earned and the grant-date fair value of all equity awards granted during the full 12-month period of fiscal year 2020 as these represent the principal forms of compensation delivered to all of our employees. Target base salary values were used for new hire employees that commenced employment in 2020 to reflect a full year of compensation. In addition, we measured compensation for purposes of determining the median coworker using the 12-month period ending December 31, 2020.

Director Compensation

The following table sets forth our 2020 non-employee director compensation program. For 2020, the Audit Committee member retainer was increased from $7,500 to $10,000; the Compensation Committee member retainers were increased from $12,500 to $15,000 and $6,000 to $7,500, for the chair and members, respectively; and the Nominating and Corporate Governance Committee member retainers were increased from $8,000 to $10,000 and $4,000 to $5,000, for the chair and members, respectively, based on a review and recommendation of market data by Compensia of peers in our industry, with these changes effective as of the date of the 2020 Annual Meeting.

Annual Cash Compensation Elements	Amount
Board Retainer	$ 40,000
Audit Committee Retainer (chair/member)	$20,000 / $10,000
Compensation Committee Retainer (chair/member)	$15,000 / $7,500
Nominating and Corporate Governance Committee Retainer (chair/member)	$10,000 / $5,000
Additional Retainer for Non-Executive Chair	$ 60,000

All retainers are paid quarterly in arrears and, if applicable, are prorated based upon board or chair service during the calendar year. In addition, we reimburse our directors for their reasonable out-of-pocket expenses to attend board and committee meetings.

In order to further align our director compensation program with stockholder interests, under our annual compensation program, directors also receive an annual equity grant on the date of each annual meeting of stockholders. The grant date fair value of the annual equity awards is equal to approximately $480,000 and the annual equity award is expected to be delivered 70% in the form of stock options and 30% in the form of RSUs. The stock options are scheduled to vest in 12 monthly installments, while the restricted stock units are scheduled to vest on the one-year anniversary of the grant date, subject in each case to earlier vesting if the annual meeting precedes the one-year anniversary of the grant date. For 2020, the annual equity grants were increased from $230,000 in 2019, based on a review and recommendation of market data by Compensia of peers in our industry, effective as of the date of the 2020 Annual Meeting.

The director compensation program also contemplates that newly appointed directors will receive an initial equity award with a grant date fair value of approximately $720,000, to be delivered with the same stock option and RSU mix as the annual equity awards. The initial stock option grants are scheduled to vest on a monthly basis over 12 months and the RSU awards are scheduled to vest on the one-year anniversary of the grant date, subject in each case to earlier vesting if the annual meeting precedes the one-year anniversary of the grant date. For 2020, the initial equity grants were increased from $460,000 in 2019, based on a review and recommendation of market data by Compensia of peers in our industry, effective for directors appointed following the 2020 Annual Meeting.

2020 Director Compensation Table

The following table sets forth information for the year ended December 31, 2020 regarding the compensation awarded to, earned by or paid to our non-employee directors.

Name	Fees Earned or Paid in Cash ($)	Stock Awards (1)(2) ($)	Option Awards (2)(3) ($)	All Other Compensation ($)	Total ($)
Klaus Veitinger, M.D., Ph.D., M.B.A.	$ 109,106	$ 144,000	$ 336,000	$ —	$ 589,106
Robert J. Alpern, M.D.	44,553	144,000	336,000	—	524,553
David Bonita, M.D.	67,317	144,000	336,000	—	547,317
Sandra I. Coufal, M.D.	46,829	144,000	336,000	—	526,829
Kathryn Falberg	60,000	144,000	336,000	—	540,000
David Hirsch, M.D., Ph.D.	55,711	144,000	336,000	—	535,711

(1) Amounts reported in this column reflect the grant date fair value of each equity award computed in accordance with FASB ASC Topic 718, Compensation-Stock Compensation, excluding estimated forfeitures. The amounts reported are calculated based on the Company's closing stock price on the date of grant multiplied by the number of shares subject to the restricted stock unit award.

(2) As of December 31, 2020, our non-employee directors had equity awards outstanding with respect to the following number of shares: Dr. Veitinger - RSUs, 5,670 and stock options, 141,170; Dr. Alpern - RSUs, 5,670 and stock options, 52,604; Dr. Bonita - RSUs, 5,670 and stock options, 43,182; Dr. Coufal - RSUs, 5,670 and stock options, 43,182; Ms. Falberg - RSUs, 5,670 and stock options, 95,945; and Dr. Hirsch - RSUs, 5,670 and stock options, 43,182.

(3) Amounts reported in this column reflect the aggregate grant date fair value of stock options awarded in 2020, computed in accordance with FASB ASC Topic 718, Compensation-Stock Compensation based on the following assumptions: risk-free interest rate of 0.4%; expected volatility of 69.1%; expected term of 5.3 years and expected dividend rate of 0%.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information relating to the beneficial ownership of our common stock as of February 19, 2021, by:

- each person, or group of affiliated persons, known by us to beneficially own more than five percent (5%) of our outstanding shares of common stock;
- each of our directors;
- each of our named executive officers; and
- all our current directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of February 19, 2021, through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 50,244,465 shares of our common stock outstanding as of February 19, 2021. Shares of our common stock that a person has the right to acquire within 60 days of February 19, 2021, are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group.

Unless otherwise indicated below, the address for each beneficial owner listed is c/o Tricida, Inc., at 7000 Shoreline Court, Suite 201, South San Francisco, CA 94080.

The below beneficial ownership table is reported as of February 19, 2021.

Name of Beneficial Owner	Shares of Common Stock Beneficially Owned	Percentage of Outstanding Shares Beneficially Owned
5% Stockholders		
OrbiMed Private Investments V, LP[(1)]	9,614,280	19.1 %
Sibling Capital[(2)]	6,423,493	12.8 %
Morgan Stanley[(3)]	4,535,138	9.0 %
Longitude Venture Partners II, L.P.[(4)]	3,019,734	6.0 %
Redmile Group, LLC[(5)]	2,858,415	5.7 %
The Vanguard Group[(6)]	2,511,612	5.0 %
Directors and Named Executive Officers		
Gerrit Klaerner, Ph.D.[(7)]	2,041,423	4.1 %
Robert J. Alpern, M.D.[(8)]	189,994	*
David P. Bonita, M.D.[(9)]	9,662,973	19.2 %
Sandra I. Coufal, M.D.[(10)]	6,628,474	13.2 %
Kathryn Falberg[(11)]	133,035	*
David Hirsch, M.D., Ph.D.[(12)]	3,068,427	6.1 %
Robert McKague[(13)]	220,933	*
Geoffrey M. Parker[(14)]	765,071	1.5 %
Dawn Parsell, Ph.D.[(15)]	439,068	*
Wilhelm Stahl, Ph.D.[(16)]	403,208	*
Klaus Veitinger, M.D., Ph.D., M.B.A.[(17)]	249,569	*
All directors and executive officers as a group (11 persons)[(18)]	23,802,175	47.4 %

* Indicates beneficial ownership of less than one percent (1%) of the outstanding shares of our common stock..

(1) Consists of 9,614,280 shares of common stock, all shares are held directly by OrbiMed Private Investments V, LP, or OPI V. OrbiMed Capital GP V LLC, or OrbiMed GP, is the sole general partner of OPI V, and OrbiMed Advisors LLC, or OrbiMed Advisors, a registered investment adviser under the Investment Advisors Act of 1940, as amended, is the managing member of OrbiMed GP. By virtue of such relationships, OrbiMed GP and OrbiMed Advisors may be deemed to have voting and investment power with respect to the shares held by OPI V noted above and as a result may be deemed to beneficially own such securities for purposes of Rule 13d-3 under the Exchange Act. OrbiMed Advisors exercises investment and voting power through a management committee comprised of Carl L. Gordon, Ph.D., Sven H. Borho and Jonathan T. Silverstein, each of whom disclaims beneficial ownership of the shares held by OPI V. David P. Bonita, M.D., a member of OrbiMed Advisors, serves on our board of directors. Each of OrbiMed GP, OrbiMed Advisors, Dr. Gordon, Mr. Borho, Mr. Silverstein, and Dr. Bonita disclaims beneficial ownership of the shares held by OPI V, except to the extent of its or his proportionate pecuniary interest therein, if any. The address of OrbiMed Advisors is 601 Lexington Avenue, 54th floor, New York, New York 10022.

(2) Consists of (a) 777,411 shares of common stock held by Sibling Capital Fund II-A L.P., or Sibling A, (b) 2,773,350 shares of common stock held by Sibling Capital Fund II-B L.P., or Sibling B, (c) 1,810,195 shares of common stock held by Sibling Capital Fund II-C L.P., or Sibling C, (d) 599,379 shares of common stock held by Sibling Capital Fund II-D L.P., or Sibling D, and (e) 463,158 shares of common stock held by Sibling Insiders Fund II L.P., or Sibling Insiders Fund, and together with Sibling A, Sibling B, Sibling C and Sibling D, the Sibling Funds. Sibling Capital Ventures LLC, or SCV, is the sole general partner of Sibling A. Sibling Capital Ventures II LLC, or SCV II, is the sole general partner of Sibling B. Sibling Capital Ventures III LLC, or SCV III, is the sole general partner of Sibling C. Sibling Capital Ventures IV LLC, or SCV IV, is the sole general partner of Sibling D. Sibling Insiders II LLC, or Sibling Insiders LLC, is the sole general partner of Sibling Insiders Fund. Each of Sandra I. Coufal, M.D. and Brian M. Isern, the brother of Dr. Coufal, is co-manager of SCV, SCV II, SCV III, SCV IV, and Sibling Insiders LLC and, as such, may be deemed to have voting and investment power with respect to the shares held by the Sibling Funds. Each of SCV, SCV II, SCV III, SCV IV, Sibling Insiders LLC, Dr. Coufal and Mr. Isern disclaims beneficial ownership of shares held by the Sibling Funds, except to the extent of its, her or his proportionate pecuniary interest therein, if any. The address of SCV, SCV II, SCV III, SCV IV, Sibling Insiders LLC and Mr. Isern is 2033 6th Ave, Suite 330, Seattle, Washington 98121.

(3) Based on a Schedule 13G filed on February 12, 2021, for the year ended December 31, 2020, by Morgan Stanley and affiliated entities, reporting shared voting power and shared dispositive power over 4,535,138 shares. Morgan Stanley & Co. LLC reported shared voting power and shared dispositive power over 2,686,063 shares. Morgan Stanley Capital Services LLC reported shared voting power and shared dispositive power over 1,103,073 shares. The address of Morgan Stanley, Morgan Stanley & Co. LLC and Morgan Stanley Capital Services LLC is 1585 Broadway, New York, New York 10036.

(4) Consists of 3,019,734 shares of common stock, all shares are held directly by Longitude Venture Partners II, L.P. (“LVPII”). Longitude Capital Partners II, LLC (“LCP II”) is the general partner of LVP II and may be deemed to have voting and investment power over the shares of the Company held by LVP II. Patrick G. Enright and Juliet Tammenoms Bakker are managing members of LCP II and may be deemed to share voting and investment power over the shares held by LVP II. David Hirsch, M.D., Ph.D. is a member of LCP II and may be deemed to share voting and investment power over the shares of the Company held by LVP II. Each of these individuals disclaims beneficial ownership of such shares except to the extent of his or her pecuniary interest therein. The address of LCPII is 2740 Sand Hill Road, Menlo Park, California 94025.

(5) Based on a Schedule 13F as of September 30, 2020.

(6) Based on a Schedule 13F as of September 30, 2020.

(7) Consists of (a) 491,993 shares of common stock held by Gerrit Klaerner, Ph.D., (b) 25,323 shares of common stock held by the spouse of Dr. Klaerner, and (c) 1,524,107 shares of common stock issuable upon exercise of stock options held by Dr. Klaerner that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 1,044,906 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below. Excludes shares held by members of Dr. Klaerner’s family who do not live in the same household as Dr. Klaerner. Dr. Klaerner disclaims beneficial ownership of shares held by members of Dr. Klaerner’s family who do not live in the same household as Dr. Klaerner. Excludes 8,000 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Klaerner that do not vest within 60 days of February 19, 2021.

(8) Consists of (a) 137,390 shares of common stock held by Robert J. Alpern, M.D. and (b) 52,604 shares of common stock issuable upon exercise of stock options held by Dr. Alpern that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 48,776 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below. Excludes 5,670 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Alpern that do not vest within 60 days of February 19, 2021.

(9) Consists of (a) 5,511 shares of common stock held by David P. Bonita, M.D. (b) 43,182 shares of common stock issuable upon exercise of stock options held by Dr. Bonita that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 39,354 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below and (c) 9,614,280 shares beneficially owned by OPI V as set forth in footnote (1). Dr. Bonita disclaims beneficial ownership of the shares listed in footnote (1), except to the extent of his proportionate pecuniary interest therein, if any. The business address for Dr. Bonita is c/o OrbiMed Advisors LLC, 601 Lexington Avenue, 54th floor, New York, New York 10022. Excludes 5,670 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Bonita that do not vest within 60 days of February 19, 2021.

(10) Consists of (a) 156,939 shares of common stock held by Sandra I. Coufal, M.D., (b) 4,860 shares held by the Coufal Irrevocable Trust, of which the spouse of Dr. Coufal is the sole trustee, (c) 43,182 shares of common stock issuable upon exercise of stock options held by Dr. Coufal that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 39,354 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below and (d) 6,423,493 shares beneficially owned by entities affiliated with Sibling Capital, as set forth in footnote (2). Dr. Coufal disclaims beneficial ownership of the shares listed in footnote (2), except to the extent of her proportionate pecuniary interest therein, if any. Dr. Coufal disclaims beneficial ownership of the shares held by the Coufal Irrevocable Trust, as to which Dr. Coufal does not exercise voting or dispositive power. The business address for Dr. Coufal is 18313 Calle La Serra, Rancho Santa Fe, California 92091-0119. Excludes 5,670 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Coufal that do not vest within 60 days of February 19, 2021.

(11) Consists of (a) 37,090 shares of common stock held by Kathryn Falberg and (b) 95,945 shares of common stock issuable upon exercise of stock options held by Ms. Falberg that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 90,651 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below. Excludes 5,670 shares of common stock issuable upon vesting and settlement of restricted stock units held by Ms. Falberg that do not vest within 60 days of February 19, 2021.

(12) Consists of (a) 5,511 shares of common stock held by David Hirsch, M.D., Ph.D., (b) 43,182 shares of common stock issuable upon exercise of stock options held by David Hirsch, M.D., Ph.D. that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 39,354 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below and (c) 3,019,734 shares beneficially owned by LVP II as set forth in footnote (4). Dr. Hirsch disclaims beneficial ownership of the shares listed in footnote (4), except to the extent of his pecuniary interest therein, if any. The business address for Dr. Hirsch is 2740 Sand Hill Road, Menlo Park, California 94025. Excludes 5,670 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Hirsch that do not vest within 60 days of February 19, 2021.

(13) Consists of (a) 10,933 shares of common stock held by Robert McKague and (b) 210,000 shares of common stock issuable upon exercise of stock options held by Mr. McKague that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 56,875 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below. Excludes 4,000 shares of common stock issuable upon vesting and settlement of restricted stock units held by Mr. McKague that do not vest within 60 days of February 19, 2021.

(14) Consists of (a) 242,837 shares of common stock held by Geoffrey M. Parker and (b) 522,234 shares of common stock issuable upon exercise of stock options held by Mr. Parker that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 368,317 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below. Excludes 4,000 shares of common stock issuable upon vesting and settlement of restricted stock units held by Mr. Parker that do not vest within 60 days of February 19, 2021.

(15) Consists of (a) 1,039 shares of common stock held by Dawn Parsell, Ph.D. and (b) 438,029 shares of common stock issuable upon exercise of stock options held by Dr. Parsell that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 245,269 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below. Excludes 4,000 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Parsell that do not vest within 60 days of February 19, 2021.

(16) Consists of (a) 15,478 shares of common stock held by Wilhelm Stahl, Ph.D. and (b) 387,730 shares of common stock issuable upon exercise of stock options held by Dr. Stahl that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 320,332 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below. Excludes 4,000 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Stahl that do not vest within 60 days of February 19, 2021.

(17) Consists of (a) 5,511 shares of common stock held by Klaus Veitinger, M.D., Ph.D., M.B.A., (b) 141,170 shares of common stock issuable upon exercise of stock options held by Dr. Veitinger that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 130,528 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are eligible for early exercise as described in footnote (18) below, (c) 51,444 shares of common stock held by the Sigrun R. Veitinger 2016 Irrevocable Trust, or the SRV Trust, for which a third-party serves as trustee, and (d) 51,444 shares of common stock held by Klaus R. Veitinger 2016 Children's Trust, or the KRV Children's Trust, for which a third-party serves as trustee. Dr. Veitinger disclaims beneficial ownership of the shares held by the SRV Trust and the KRV Children's Trust, except to the extent of his proportionate pecuniary interest therein, if any. Excludes 5,670 shares of common stock issuable upon vesting and settlement of restricted stock units held by Dr. Veitinger that do not vest within 60 days of February 19, 2021.

(18) Consists of (a) all shares of common stock held by our directors and executive officers and (b) all shares of common stock issuable upon exercise of stock options held by our directors and five current executive officers that are exercisable as of February 19, 2021 or will become exercisable within 60 days of such date, 2,423,716 of which have vested, or will vest, within 60 days of February 19, 2021, the remainder of which are unvested but may be exercised prior to vesting subject to a repurchase arrangement with us, as described further below. Twenty five percent (25%) of the shares issuable upon exercise of options granted to our directors and executive officers vest on the first anniversary of the applicable vesting commencement date and in subsequent 1/48th increments each subsequent month thereafter, subject to continuous service as of each vesting date. Our directors and executive officers may elect to early exercise their options at any time prior to vesting, provided that the shares issued upon exercise of the unvested options will be shares of restricted stock subject to our right to repurchase the shares, should the applicable director or executive officer cease to serve as a director or employee of us prior to the full vesting of such shares of restricted stock. In addition, vesting of an executive officer's then outstanding and unvested option will accelerate upon termination of service in connection with a change in control, as provided in our executive severance benefit plan.

Equity Compensation Plan Information

The following table summarizes the number of outstanding options and restricted stock units granted to our employees, consultants, and directors, as well as the number of shares of common stock remaining available for future issuance, under our equity compensation plans as of December 31, 2020.

	Number of securities to be issued upon exercise of outstanding options	Weighted average exercise price of outstanding options	Number of securities remaining available for future issuance
Equity compensation plans approved by security holders	8,120,435(1)	$19.25(2)	4,053,582(3)
Equity compensation plans not approved by security holders	—	—	—
Total	8,120,435	$ 19.25	4,053,582

(1) Includes 90,020 restricted stock units that were outstanding on December 31, 2020 under the Company's 2018 Equity Incentive Plan. Restricted stock unit awards may be settled only for shares of common stock on a one-for-one basis.
(2) Only option awards were used in computing the weighted-average exercise price.
(3) This amount represents shares of common stock available for issuance under the Company's 2018 Equity Incentive Plan. Awards available for grant under the Company's 2018 Equity Incentive Plan include stock options, stock appreciation rights, restricted stock, restricted stock units, other stock awards, performance awards, and any combination of the foregoing awards. This number also includes 1,605,123 shares available under our Employee Stock Purchase Plan ("ESPP"). The ESPP provides the opportunity for eligible coworkers to acquire shares of our common stock at a discount. The number of shares of our common stock reserved for issuance under our 2018 Equity Incentive Plan will automatically increase on the first day of each fiscal year by the lesser of 4% of the number of shares of common stock outstanding on the first day of such fiscal year, 3,200,000 shares of our common stock or such lesser amount as is determined by our board of directors. The number of shares of our common stock reserved for issuance under our ESPP will automatically increase on the first day of each fiscal year by the lesser of 1% of the number of shares of common stock outstanding on the first day of such fiscal year, 800,000 shares of our common stock or such lesser amount as is determined by our board of directors.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

Certain Relationships and Related Person Transactions

Our audit committee is responsible for reviewing and approving, prior to our entry into any such transaction, all related person transactions. In addition, our Code of Business Conduct and Ethics requires that our officers and employees avoid taking for themselves personally opportunities that are discovered through the use of our property, information or position or use of our property, information or position for personal gain.

A related person transaction includes transactions in which:

- we have been or are to be a participant;
- the amounts involved exceeded or will exceed $120,000; and
- any of our directors, executive officers or holders of more than five percent (5%) of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest.

A related person transaction does not include the compensation arrangements with our directors and executive officers that are described elsewhere in this Annual Report on Form 10-K. There have not been any related person transactions since January 1, 2020.

Independence of Directors

The information required under this Item regarding the independence of directors is discussed above under "Item 10—Corporate Governance—Director Independence."

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Audit Committee Report

The audit committee oversees our independent registered public accounting firm and assists our board of directors in fulfilling its oversight responsibilities on matters relating to our accounting and financial reporting processes, the integrity of our financial statements, our compliance with legal and regulatory requirements and the independent registered public accounting firm's qualifications and independence by meeting regularly with the independent registered public accounting firm and financial management personnel. Management is responsible for the preparation, presentation and integrity of our financial statements.

In fulfilling its oversight responsibilities, the audit committee:

- reviewed and discussed our financial statements as of and for the fiscal year ended December 31, 2020 with management and Ernst & Young LLP our independent registered public accounting firm;
- discussed with Ernst & Young LLP the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board and the SEC;
- received the written disclosures and the letter from Ernst & Young LLP required by the applicable requirements of the Public Company Accounting Oversight Board; and
- discussed the independence of Ernst & Young LLP with that firm.

Based on the audit committee's review and discussions noted above, the audit committee recommended to our board of directors, and our board of directors approved, that the audited financial statements be included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 for filing with the SEC. The audit committee also appointed Ernst & Young LLP as our independent registered public accounting firm for fiscal year ending December 31, 2021.

Submitted by the audit committee of our board of directors:

Kathryn Falberg, Chairperson
David Bonita, M.D.
David Hirsch, M.D., Ph.D.

Principal Accountant Fees and Services

We were billed by EY for the years ended December 31, 2020 and 2019 as follows:

	Years Ended December 31,	
	2020	2019
Audit fees	$ 1,714,347	$1,975,782
Audit-related fees	—	—
Tax fees	—	—
All other fees	—	—
Total fees	$ 1,714,347	$1,975,782

Audit fees above are professional services associated with the integrated audit of our financial statements and the filing of our registration statements. There are no audit-related or tax fees billed by EY in years ended December 31, 2020 and 2019.

Determination of Independence

In considering the nature of the services provided by our independent registered public accounting firm, the audit committee determined that such services are compatible with the provision of independent audit services. The audit committee discussed these services with our independent registered public accounting firm and our management to determine that they are permitted under the rules and regulations concerning auditor independence.

Additional information concerning the audit committee and its activities can be found: “Committee of the Board of Directors” and “Audit Committee Report.”

Pre-Approval Policy

According to policies adopted by the audit committee and ratified by our board of directors, to ensure compliance with the SEC’s rules regarding auditor independence, all audit and non-audit services to be provided by our independent registered public accounting firm must be pre-approved by the audit committee. The audit committee has established a general pre-approval policy for certain audit and non-audit services, up to a specified amount for each identified service that may be provided by the independent auditors. The audit committee may delegate pre-approval authority to one or more of its members. Kathryn Falberg is currently designated as the member to whom such authority is delegated, and she must report, for informational purposes only, any pre-approval decisions to the audit committee at or prior to its next scheduled meeting.

The audit committee approved one hundred percent (100%) of all services provided by EY during the years ended December 31, 2020 and 2019. The audit committee has considered the nature and amount of the fees billed by EY and believes that the provision of the services for activities unrelated to the audit is compatible with maintaining EY’s independence.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a)

(1) Financial Statements

The financial statements filed as part of this report are included in Part II, Item 8. of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

Financial statement schedules have been omitted as the information required is not applicable or the information is presented in the financial statements and related notes included in Part II, Item 8. of this Annual Report on Form 10-K.

(b) Exhibits

EXHIBIT INDEX

Exhibit Number	Exhibit Description
3.1	Amended and Restated Certificate of Incorporation of Registrant, as currently in effect (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed on June 16, 2020).
3.2	Bylaws of Registrant, as currently in effect (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K filed on July 2, 2018).
4.1	Amended and Restated Investor Rights Agreement among the Registrant and certain of its stockholders, dated November 7, 2017, as amended (incorporated by reference to Exhibit 4.1 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
4.2	Amendment No. 1 to Amended and Restated Investor Rights Agreement among the Registrant and certain of its stockholder, dated February 28, 2018 (incorporated by reference to Exhibit 4.2 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
4.3	Specimen common stock certificate of the Registrant (incorporated by reference to 4.3 to the Registration Statement on form S-1 (333-225420), Amendment No. 2 filed on June 25, 2018).
4.4	Warrant Agreement to Purchase Shares of Common Stock, dated February 28 2018, between the Registrant and Hercules Capital, Inc. (incorporated by reference to Exhibit 4.5 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
4.5	Warrant Agreement to Purchase Shares of Common Stock, dated February 28, 2018, between the Registrant and Hercules Technology III, L.P. (incorporated by reference to Exhibit 4.6 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
4.6	Warrant Agreement to Purchase Shares of Common Stock of the Company, dated as of December 28, 2018 (incorporated by reference to Exhibit 4.1 to the Current report on Form 8-K filed on January 3, 2019).
4.7	Warrant Agreement to Purchase Shares of Common Stock of the Company, dated as of March 27, 2019 (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed on March 28, 2019).
4.8	Warrant Agreement to Purchase Shares of Common Stock of the Company, dated as of March 27, 2019 (incorporated by reference to Exhibit 4.2 to the Current Report on Form 8-K filed on March 28, 2019).
4.9	Warrant Agreement to Purchase Shares of Common Stock of the Company, dated as of December 13, 2019 (incorporated by reference to Exhibit 4.9 to the Annual Report on Form 10-K filed on March 2, 2020).

4.10	Warrant Agreement to Purchase Shares of Common Stock of the Company, dated as of May 19, 2020 (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on May 19, 2020).
4.11	Warrant Agreement to Purchase Shares of Common Stock of the Company, dated as of May 19, 2020 (incorporated by reference to Exhibit 10.3 to the Current Report on Form 8-K filed on May 19, 2020).
4.12	Indenture, dated May 22, 2020, between Tricida, Inc. and U.S. Bank National Association, including the form of 3.50% Convertible Senior Notes due 2027 (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed on May 22, 2020).
4.13*	Description of the Company's Common Stock, $0.001 par value.
10.1^	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-1 (333-225420), Amendment No. 2 filed on June 25, 2018).
10.2^	2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registration Statement on Form S-1 (333-225420), Amendment No. 2 filed on June 25, 2018).
10.3^	Form of Director Restricted Stock Unit Award Agreement (annual grant) (incorporated by reference to Exhibit 10.4 to the Registration Statement on Form S-1 (333-225420), Amendment No. 2 filed on June 25, 2018).
10.4^	Form of Director Stock Option Agreement (annual grant) (incorporated by reference to Exhibit 10.5 to the Registration Statement on Form S-1 (333-225420), Amendment No. 2 filed on June 25, 2018).
10.5^	Employee Stock Purchase Plan (as amended and restated on June 11, 2020) (incorporated by reference to Exhibit 10.4 to the Quarterly Report on Form 10-Q filed on August 6, 2020).
10.6	Loan and Security Agreement, dated February 28, 2018, among the Registrant, Hercules Capital, Inc. and the several banks and other financial institutions or entities from time to time parties thereto (incorporated by reference to Exhibit 10.6 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
10.7	First Amendment to Loan and Security Agreement and First Amendment to Warrants, dated as of April 10, 2018, among the Registrant, Hercules Capital, Inc. and the several banks and other financial institutions or entities from time to time parties thereto (incorporated by reference to Exhibit 10.7 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
10.8	Second Amendment to Loan and Security Agreement, dated as of October 15, 2018, among the Registrant, Hercules Capital, Inc. and the several banks and other financial institutions or entities from time to time parties thereto (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on October 18, 2018).
10.9	Third Amendment to Loan and Security Agreement, dated as of March 27, 2019 among Tricida Inc., Hercules Capital, Inc. and the several banks and other financial institutions or entities from time to time parties thereto (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on March 28, 2019).
10.10	Fourth Amendment to Loan and Security Agreement, dated as of March 31, 2020 among Tricida Inc., Hercules Capital, Inc. and the several banks and other financial institutions or entities from time to time parties thereto (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed on May 8, 2020).
10.11	Fifth Amendment to Loan and Security Agreement, dated as of May 18, 2020 among Tricida, Inc., Hercules Capital Inc. and the several banks and other financial institutions or entities from time to time parties thereto (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on May 19, 2020).
10.12	Sixth Amendment to Loan and Security Agreement, dated as of January 6, 2021 among Tricida, Inc., Hercules Capital Inc. and the several banks and other financial institutions or entities from time to time parties thereto (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on January 11, 2021).
10.13	Lease Agreement, dated April 4, 2014, between the Registrant and ARE-San Francisco No. 17, LLC (incorporated by reference to Exhibit 10.8 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).

10.14	First Amendment to Lease, dated August 2, 2017, between the Registrant and ARE-San Francisco No. 17, LLC (incorporated by reference to Exhibit 10.9 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
10.15	Second Amendment to Lease, dated November 7, 2017, between the Registrant and ARE-San Francisco No. 17, LLC (incorporated by reference to Exhibit 99.1 to the Current report on Form 8-K filed on August 19, 2019).
10.16	Third Amendment to Lease, dated August 14, 2019, between the Registrant and ARE-San Francisco No. 17, LLC (incorporated by reference to Exhibit 10.1 to the Current report on Form 8-K filed on August 19, 2019).
10.17*	Fourth Amendment to Lease, dated December 14, 2020, between the Registrant and ARE-San Francisco No. 17, LLC.
10.18+	Master Development/Validation Services and Clinical/Launch Supply Agreement (incorporated by reference to Exhibit 10.10 to the Registration Statement on Form S-1 (333-225420) filed on June 4, 2018).
10.19†*	Manufacturing and Commercial Supply Agreement with Patheon Austria GmbH & Co KG, dated October 4, 2019 (incorporated by reference to Exhibit 10.15 to the Annual Report on Form 10-K filed on March 2, 2020).
10.20^	Tricida, Inc. Annual Incentive Plan (incorporated by reference to Exhibit 10.1 to the Current report on Form 8-K filed on February 22, 2019).
10.21^	Form of Tricida, Inc. Executive Severance Benefit Plan, as amended (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on February 28, 2020).
10.22^	Tricida, Inc. Executive Retention Agreement Template (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed on November 9, 2020).
10.23^	Tricida, Inc. 2020 Inducement Plan (incorporated by reference to Exhibit 4.3 to the Registration Statement on Form S-8 filed on January 8, 2021).
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1*	Power of Attorney (included on the signature page).
31.1*	Certification of Chief Executive Officer pursuant to Exchange Act Rule 13a-14(a) or 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act.
31.2*	Certification of Chief Financial Officer pursuant to Exchange Act Rule 13a-14(a) or 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act.
32.1**	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	XBRL Instance Taxonomy.
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 Labels Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.
104*	Inline XBRL for the cover page of this Annual Report on Form 10-K included in the Exhibit 101.

*	Filed herewith.
**	Furnished herewith.
^	Management contracts and compensation plans and arrangements.
+	Confidential treatment with respect to specific portions of this Exhibit has been granted, and such portions are omitted and have been filed separately with the Securities and Exchange Commission.
†	Certain portions of this exhibit ((indicated by “[***]”) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K because they are not material and would likely cause competitive harm to the registrant if publicly disclosed.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

TRICIDA, INC.

Dated: February 26, 2021

TRICIDA, INC.

By: /s/ Gerrit Klaerner

Name: Gerrit Klaerner, Ph.D.
Title: Chief Executive Officer and President

SIGNATURES AND POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Gerrit Klaerner and Geoffrey M. Parker, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

SIGNATURE		DATE
/s/ Gerrit Klaerner Gerrit Klaerner, Ph.D.	Chief Executive Officer, President and Director (Principal Executive Officer)	February 26, 2021
/s/ Geoffrey M. Parker Geoffrey M. Parker	Chief Operating Officer, Chief Financial Officer and Executive Vice President (Principal Financial Officer)	February 26, 2021
/s/ Annie Yoshiyama Annie Yoshiyama	Vice President of Finance and Chief Accounting Officer (Principal Accounting Officer)	February 26, 2021
/s/ Klaus Veitinger Klaus Veitinger, M.D., Ph.D., M.B.A.	Chairman of the Board of Directors	February 26, 2021
/s/ Robert J. Alpern Robert J. Alpern, M.D.	Director	February 26, 2021
/s/ David Bonita David Bonita, M.D.	Director	February 26, 2021
/s/ Sandra I. Coufal Sandra I. Coufal, M.D.	Director	February 26, 2021
/s/ Kathryn Falberg Kathryn Falberg	Director	February 26, 2021
/s/ David Hirsch David Hirsch, M.D., Ph.D.	Director	February 26, 2021

MANAGEMENT

Gerrit Klaerner, PhD
Founder, Chief Executive Officer & President

Robert McKague, JD
EVP, General Counsel & Chief Compliance Officer

Geoffrey Parker
EVP, Chief Operating Officer & Chief Financial Officer

Dawn Parsell, PhD
EVP, Clinical Development

Wilhelm Stahl, PhD
EVP, Chief Technology Officer

BOARD OF DIRECTORS

Klaus Veitinger, MD, PhD
Chairman of the Board
Venture Partner, OrbiMed Advisors, LLC

Robert J. Alpern, MD
Dean (retired) and Ensign Professor,
Yale School of Medicine

David Bonita, MD
Private Equity Partner, OrbiMed Advisors, LLC

Sandra I. Coufal, MD
Manager, Sibling Capital Ventures LLC

Kathryn Falberg
Director

David Hirsch, MD, PhD
Managing Director, Longitude Capital

Gerrit Klaerner, PhD
Founder, Chief Executive Officer & President

CORPORATE INFORMATION

Tricida, Inc.
7000 Shoreline Court, Suite 201
South San Francisco, California 94080
415.429.7800
info@tricida.com

ANNUAL MEETING

June 10, 2021 at 7:30 a.m. Pacific Time
Held in a virtual meeting format only at
www.virtualshareholdermeeting.com/TCDA2021

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Ernst & Young LLP

CORPORATE COUNSEL

Sidley Austin LLP

STOCK INFORMATION

Our common stock is traded on
The Nasdaq Global Select Market
under the symbol **TCDA**

TRANSFER AGENT

Computershare
PO Box 505000
Louisville, Kentucky 40233-5000
United States

Overnight delivery:
462 South 4th Street, Suite 1600
Louisville, Kentucky 40202
United States

Phone:
Toll free: 800.962.4284
Toll: +1.781.575.4247

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