Altus Pharmaceuticals Inc.
Form 10-K
March 11, 2009

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

FORM 10-K

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2008

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission File No. 000-51711

ALTUS PHARMACEUTICALS INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**04-3573277**
(State or Other Jurisdiction of Incorporation or Organization)	*(I.R.S. Employer Identification No.)*
333 Wyman Street, Waltham, Massachusetts	**02451**
(Address of Principal Executive Offices)	*(Zip Code)*

Registrant s telephone number, including area code:
(781) 373-6000

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $.01 par value	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act:
NONE
(Title of Class)

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

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 o NO þ

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 þ NO o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

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

Large accelerated filer o Accelerated filer þ Non-accelerated filer o Smaller reporting company o
(Do not check if a smaller reporting company)

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold on The Nasdaq Global Market on June 30, 2008 was $137,373,943.

The number of shares outstanding of the registrant s common stock as of March 6, 2009 was 31,131,056.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required in Part III of this Annual Report on Form 10-K will be incorporated either from the registrant s definitive Proxy Statement for the registrant s Annual Meeting of Stockholders to be held on June 17, 2009, or from a future amendment to this Form 10-K, to be filed with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year covered by this Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The forward-looking statements are contained principally in, but not limited to, the sections entitled Business, Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations. These statements involve known and unknown risks, uncertainties and other important factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the expected timing, progress or success of our preclinical research and development and clinical programs;
- the anticipated effects and expected costs of the strategic realignment we have announced, including the workforce reductions;
- the amount of time that our existing cash resources will fund operating expenses, the transition of the Trizytek program to the Cystic Fibrosis Foundation Therapeutics, Inc., or CFFTI, and the future of the Trizytek program;
- our ability to raise sufficient capital to fund our operations;
- our ability to successfully obtain sufficient supplies of our product candidates for use in clinical trials and toxicology studies and secure sufficient commercial supplies of our product candidates;
- the timing, costs and other limitations involved in obtaining regulatory approval for any of our product candidates;
- the potential benefits of our product candidates over other therapies;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates that we are developing or may develop in the future;
- our estimate of market sizes and anticipated uses of our product candidates;
- our ability to enter into and maintain collaboration agreements with respect to our product candidates and the performance of our collaborative partners under such agreements;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our estimates of future performance; and
- our estimates regarding anticipated operating losses, future revenue, expenses, capital requirements and our needs for additional financing.

In some cases, you can identify forward-looking statements by terms such as anticipate, assume, believe, could, estimate, expect, intend, may, plan, potential, predict, project, should, will, would and similar identify forward-looking statements. Forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Because of these risks and uncertainties,

the forward-looking events and circumstances discussed in this Annual Report on Form 10-K may not transpire. We discuss many of these risks in Item 1A of this Annual Report on Form 10-K under the heading Risk Factors beginning on page 27.

Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our estimates and assumptions only as of the date of this document. You should read this document and the documents that we reference in this Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. Except as required by law, we do not undertake any obligation to update or revise any forward-looking statements contained in this Annual Report on Form 10-K, whether as a result of new information, future events or otherwise.

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PART I

ITEM 1. *BUSINESS*

Our Corporate Information

We were incorporated in Massachusetts in October 1992 as a wholly-owned subsidiary of Vertex Pharmaceuticals Incorporated, or Vertex, from whom we exclusively license specified patents underlying some of our product candidates. In February 1999, we were reorganized as an independent company, and in August 2001 we reincorporated in Delaware. Prior to May 2004, we were named Altus Biologics Inc. We have one subsidiary, Altus Pharmaceuticals Securities Corp., a Massachusetts corporation. Unless the context requires otherwise, references to Altus, we, our , us and the Registrant in this report refer to Altus Pharmaceuticals Inc. and our subsidiary.

Altus is a trademark of Altus Pharmaceuticals Inc. Trizytek™ [liprotamase] is a trademark that we have assigned to CFFTI. Each of the other trademarks, trade names or service marks appearing in this report belongs to its respective holder.

Business Overview

We are a biopharmaceutical company focused on the development of oral and injectable protein therapeutics. We have used our proprietary protein crystallization technology to develop protein therapies that we believe will have significant advantages over existing products and will address unmet medical needs. Our product candidates are designed to either substitute a protein that is in short supply in the body or degrade toxic metabolites in the gut and remove them from the blood stream.

On January 26, 2009, we announced a strategic realignment to focus on the advancement of our long-acting, recombinant human growth hormone candidate, ALTU-238, as a once-per-week treatment for adult and pediatric patients with growth hormone deficiency. To conserve capital resources, we are discontinuing our activities in support of Trizytek, an orally delivered enzyme replacement therapy for patients suffering from malabsorption due to exocrine pancreatic insufficiency. In addition, we are evaluating the feasibility of moving forward our early-stage clinical and pre-clinical programs and will make future decisions on these programs subject to the availability of resources. In connection with the realignment, we implemented a workforce reduction of approximately 75%, primarily in functions related to the Trizytek program as well as certain general and administrative positions.

On February 20, 2009, CFFTI and we entered into a letter agreement, or the Letter Agreement, and a license agreement, or the License Agreement, terminating our strategic alliance agreement. Under the terms of the License Agreement, we assigned the Trizytek trademark and certain patent rights to CFFTI and granted CFFTI an exclusive, worldwide, royalty-bearing license to use certain other intellectual property owned or controlled by us to develop, manufacture and commercialize any product using, in any combination, the three active pharmaceutical ingredients, or APIs, which comprise Trizytek. In these agreements, we also agreed to assist CFFTI with a transition of our on-going development and regulatory activities and clinical trials through March 27, 2009, after which CFFTI will be responsible for future development activities. In exchange, CFFTI agreed to release us from all obligations and liabilities resulting from the original strategic alliance agreement, and to pay us a percentage of any proceeds CFFTI realizes associated with respect to any rights licensed or assigned to CFFTI under the License Agreement.

Our product candidates are based on our proprietary technology, which enables the large-scale crystallization of proteins for use as therapeutic drugs. We apply our technology to improve known protein drugs, as well as to develop

other proteins into protein therapeutics. For example, we are developing our product candidate, ALTU-238, by applying our proprietary crystallization technology with the goal of offering an improved version of an approved drug. We believe that, by using our technology, we are able to overcome many of the limitations of existing protein therapies and deliver proteins in capsule and alternative dosage forms, such as a liquid oral form, and extended-release injectable formulations. Our product candidates are designed to offer improvements over existing products, such as greater convenience, better safety and efficacy

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and longer shelf life. In addition, we believe that we may be able to reduce the development risk and time to market for our drug candidates because we apply our technology to existing, well-understood proteins with well-defined mechanisms of action. We believe that our technology is broadly applicable to different classes of proteins, including enzymes, hormones, antibodies, cytokines and peptides. To date, we have crystallized more than 70 proteins for use in our research and development programs.

ALTU-238 for Growth Hormone Deficiency and Related Disorders

ALTU-238 is a crystallized formulation of human growth hormone, or hGH, that is designed to be injected once-weekly with a fine gauge needle for the treatment of growth hormone deficiency in children and adults as well as other growth disorders. Based on reported revenues of existing products, global sales of hGH products exceeded $2.8 billion in 2007. We are developing ALTU-238 for both adult and pediatric populations as an alternative to current therapies. Current medical guidelines for clinical practice generally recommend daily administration of existing therapies by subcutaneous injection. In March 2009, we plan to initiate a Phase II clinical trial for ALTU-238 in children for the treatment of growth hormone deficiency, and we have successfully completed a Phase II clinical trial of ALTU-238 in adults for the treatment of growth hormone deficiency.

In our clinical trials completed to date, ALTU-238 demonstrated pharmacokinetic and pharmacodynamic profiles that are consistent with once-weekly administration. In our completed Phase II clinical trial in growth hormone deficient adults, we identified doses of ALTU-238 that maintained insulin-like growth factor 1, or IGF-1, levels within the normal range for age and gender over the course of the study. IGF-1 is a naturally occurring hormone that stimulates the growth of bone, muscle and other body tissues in response to hGH and, in turn, regulates hGH, release from the pituitary gland. In addition, once-per-week dosing of ALTU-238 also appeared to result in a consistent, linear dose response of hGH and IGF-1 levels in the blood, which we believe will enable physicians and patients to correlate a given dose of ALTU-238 to desired levels of hGH and IGF-1 in the blood. We believe that the convenience of once-weekly administration of ALTU-238, if approved, would improve patient acceptance and compliance, and thereby effectiveness.

ALTU-237 for Treatment of Hyperoxalurias and Kidney Stones

ALTU-237 is a treatment for hyperoxalurias, a series of conditions in which excess oxalate is present in the body, resulting in an increased risk of developing kidney stones and, in rare instances, crystal formations in other organs. Increased oxalate in the body can be the result of a variety of factors including excess dietary intake of oxalate, genetic metabolite disorders, and disease states such as inflammatory bowel disease. The oxalate combines with calcium in the urine causing formations of calcium oxalate crystals, which can grow into kidney stones. Kidney stones can be a serious medical condition. Kidney stones occur in 10% of adult men and 3% of adult women during their lifetimes. There are a variety of types of kidney stones, but calcium oxalate stones are the most common type in people who have kidney stone disease. We have completed a Phase I clinical trial for ALTU-237 but further development of this product is on hold until sufficient additional funding can be secured.

Preclinical Pipeline

We also have a pipeline of product candidates in preclinical research and development that we are designing to address other areas of unmet need in gastrointestinal and metabolic disorders.

We have tested our product candidate ALTU-236 in animal models for the treatment of phenylketonuria, or PKU. PKU is a rare, inherited, metabolic disorder that results from an enzyme deficiency that causes the accumulation of the amino acid phenylalanine in the body. If left untreated, PKU can result in mental retardation, swelling of the brain, delayed speech, seizures and behavior abnormalities.

We also tested our product candidate ALTU-242 in animal models for the treatment of gout, a condition which we believe is in need of improved pharmaceutical therapies. Gout is caused by excess levels of urate in the body which can precipitate and form crystals in joints causing a painful and erosive arthritis. Gout is a common disorder that affects at least 1% of the population in Western countries and is the most common

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inflammatory joint disease in men over 40 years of age. Data suggests that there are more than 1.6 million diagnoses of gout in the United States annually.

Further development of ALTU-236 and ALTU-242 is on hold until sufficient additional funding can be secured.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on developing and commercializing protein therapies to address unmet medical needs. Our strategy to achieve this objective includes the following elements:

Focus on advancing ALTU-238. We are developing ALTU-238 as a once-per-week treatment for adult and pediatric patients with growth hormone deficiency. We believe that ALTU-238 represents a very promising opportunity to make a major impact on the multi-billion dollar market for growth hormone replacement products. As a mid-stage program with what we believe to be a relatively straight-forward path toward regulatory approval, we believe narrowing our focus to ALTU-238 will enable Altus to preserve capital and minimize clinical and regulatory risk. We believe that this product candidate, if approved, will offer significant advantages over existing therapies.

Establish collaborations with leading pharmaceutical and biotechnology companies. We intend to explore and evaluate collaborations for our product candidates with other companies with the goal of achieving several objectives including gaining greater access to a market or funding and/or accelerating the development of a product candidate. In addition, we believe that our technology has broad applicability to many classes of therapeutic proteins and can be used to enhance protein therapeutics developed by other parties. In the future we may derive value from our technology by selectively collaborating with biotechnology and pharmaceutical companies that will use our technology for products that they are either currently marketing or developing.

Our Product Candidates

ALTU-238 for Growth Hormone Deficiency and Related Disorders

ALTU-238 is a crystallized formulation of hGH that is designed to be administered once weekly through a fine-gauge needle for the treatment of hGH deficiency and related disorders in both pediatric and adult populations. Based on reported revenues of existing products, these indications generated approximately $2.8 billion in worldwide sales of hGH in 2007. We are developing ALTU-238 as a long-acting, growth hormone product that can allow patients to avoid the inconvenience of the daily injections recommended by current medical guidelines for existing products. We have used our proprietary protein crystallization technology and formulation expertise to develop ALTU-238 without altering the underlying molecule or requiring polymer encapsulation. Since hGH is a known protein therapeutic with an established record of long-term safety and efficacy, we believe that ALTU-238 may have less development risk than most pharmaceutical product candidates at a similar stage of development.

We have successfully completed four clinical trials of ALTU-238: three Phase I trials in healthy adults and a Phase II trial in growth hormone deficient adults. These trials were designed to determine the safety, pharmacokinetics and pharmacodynamics of ALTU-238. Pharmacokinetics refers to the process by which a drug is absorbed, distributed, metabolized and eliminated by the body. Pharmacodynamics refers to the process by which a drug exerts its biological effect. In our clinical trials completed to date, ALTU-238 demonstrated pharmacokinetic and pharmacodynamic parameters that are consistent with once-weekly administration.

In the adult Phase II trial, ALTU-238 demonstrated a pharmacokinetic and pharmacodynamic profile that we believe is supportive of a once-per-week dosing regimen for growth hormone deficient adults. The study identified doses of

ALTU-238 that maintained IGF-1 levels within the normal range for age and gender over the course of the study. IGF-1 is a naturally occurring hormone that stimulates the growth of bone, muscle and other body tissues in response to hGH and, in turn, regulates hGH release from the pituitary gland. The study also indicated that once-per-week dosing of ALTU-238 appeared to result in a consistent, linear dose response

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of hGH and IGF-1 levels in the blood. ALTU-238 was generally well tolerated, and there were no serious adverse events reported in either study. In March 2009, we plan to initiate a Phase II trial in growth hormone deficient pediatric patients that is designed to determine the safety, tolerability and clinical activity of ALTU-238 in this patient population.

In December 2006, we entered into a collaboration and license agreement with Genentech relating to the development, manufacture and commercialization of ALTU-238 and other pharmaceutical products containing crystallized hGH using our proprietary technology. In connection with the agreement, Genentech also purchased 794,575 shares of our common stock on February 27, 2007 for an aggregate purchase price of $15.0 million. On December 19, 2007, Genentech and we entered into an agreement terminating the collaboration effective December 31, 2007. Under the termination agreement, we reacquired the North American development and commercialization rights to ALTU-238.

Disease Background, Market Opportunity and Limitations of Existing Products

Growth hormone, which is secreted by the pituitary gland, is the major regulator of growth in the body. Growth hormone directly stimulates the areas of bones known as epiphyseal growth plates, which are responsible for bone elongation and growth. Growth hormone also causes growth indirectly by triggering the release of insulin-like growth factor 1, or IGF-1, from tissues throughout the body. In addition, growth hormone contributes to proper bone density and plays an important role in various metabolic functions, including lipid breakdown, protein synthesis and insulin regulation.

Growth hormone deficiency typically results from an abnormality within or near the hypothalamus or pituitary gland that impairs the ability of the pituitary to produce or secrete growth hormone. A deficiency of growth hormone can result in reduced growth in children and lead to short stature. Because the growth plates in the long bones fuse and additional cartilage and bone growth can no longer occur after puberty, hGH replacement therapy does not cause growth in adults. However, low levels of hGH in adults are associated with other metabolic disorders, including lipid abnormalities, decreased bone density, decreased cardiac performance and decreased muscle mass. These disorders typically become increasingly apparent after a prolonged period of hGH deficiency.

Children and adults with growth hormone deficiency are typically treated with growth hormone replacement therapy. Growth hormone is also FDA-approved and prescribed for many patients suffering from a range of other diseases or disorders, including pediatric growth hormone deficiency, adult growth hormone deficiency, being small for gestational age and idiopathic short stature in children. According to industry estimates:

- 1 in 3,500 children suffer from growth hormone deficiency;
- 1 in 10,000 adults suffer from growth hormone deficiency;
- between 3% and 10% of births annually are small for gestational age; and
- between 2% and 3% of children are affected by idiopathic short stature.

Growth hormone is also used to treat Turner syndrome, Prader Willi syndrome, Noonan syndrome, chronic renal insufficiency, AIDS wasting and short bowel syndrome. The percentage of patients for whom hGH is prescribed varies significantly by indication. We believe that a once-weekly formulation of hGH, such as ALTU-238, may result in increased use in a number of these indications.

Currently, many of the FDA-approved hGH products are also in clinical development for additional indications, including Crohn s disease, female infertility, bone regeneration and a variety of other genetic and metabolic disorders.

There are currently ten FDA-approved hGH products on the market in the United States from eight manufacturers, all of which use essentially the same underlying hGH molecule. Current medical guidelines for clinical practice generally recommend daily administration of existing products by subcutaneous injection. We believe that the primary differences between these products relate to their formulation and the devices employed for their delivery.

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We believe that the burden of frequent injections significantly impacts quality of life for both adults and children being treated with hGH therapy and often leads to reduced compliance or a reluctance to initiate therapy. For example, we estimate that a standard course of treatment for pediatric growth hormone deficient patients typically lasts approximately six years and requires more than 1,800 injections. Faced with this protracted treatment regime, pediatric patients often take days off and miss treatment. For adults with growth hormone deficiency, the benefits of hGH treatment are more subtle and relate to metabolic function and organ health instead of increased height. As a consequence, and in contrast to hGH deficient children, many adults with growth hormone deficiency do not initiate hGH therapy, and of those who do, many fail to continue treatment.

Anticipated Advantages of ALTU-238

We expect that ALTU-238, if approved, will offer patients a more convenient and effective long-term therapy because of the following features:

Convenience of once-weekly dosing. Based on the results of our Phase I and Phase II clinical trials, we believe that ALTU-238 will offer growth hormone deficient patients the convenience of a once-weekly injection. We believe this will improve acceptance and compliance and thereby increase long-term effectiveness of therapy and potentially expand the market.

Administration with a fine gauge needle. ALTU-238 is designed to provide extended release without changing the chemical structure of the hGH molecules or using polymers to encapsulate the component hGH molecules. To date, there has not been an hGH therapy approved by the FDA for administration once per week. The only hGH therapy approved by the FDA for administration less frequently than once per week was withdrawn from the market and required polymeric encapsulation for its extended release formulation. This necessitated the use of a substantially larger needle and was associated with pain and skin reactions at the injection site. We have designed ALTU-238 using our protein crystallization technology so that, as the crystals dissolve, the hGH is released over an extended period. This allows ALTU-238 to be administered with a 29 or 30 gauge, insulin-like needle.

In addition, we have designed ALTU-238 to be manufactured using well-established equipment and processes consistent with other injectable protein products. We believe this will provide flexibility in the scale-up and commercial production of ALTU-238, if approved.

ALTU-238 Development Activities and Strategy

We have completed three Phase I clinical trials of ALTU-238 in healthy adults and a Phase II clinical trial in adults with growth hormone deficiency. The pharmacokinetic and pharmacodynamic results from these trials support our view as to the appropriateness of once-weekly dosing of ALTU-238, and we believe that ALTU-238, if approved, can be administered once weekly. The results of our Phase Ic trial in healthy adults and Phase II trial in growth hormone deficient adults are summarized in the tables below. Furthermore, based on the results of these trials, we plan to initiate a Phase II trial in growth hormone deficient pediatric patients in March 2009, which is designed to determine the safety, tolerability and clinical activity of ALTU-238 in this patient population.

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Phase Ic Clinical Trial

ALTU-238 Phase Ic Clinical Trial Summary

Title	A Randomized, Open Label, Single Center Study to Assess the Pharmacokinetics, Pharmacodynamics, and Safety of ALTU-238 (Somatropin) in Normal Healthy Adult Males
Design	Thirty-six subjects received one of the following treatment regimens:
Administration	a single injection of ALTU-238 at a dose of 8.8 mg, 16.9 mg or 25.0 mg of hGH, administered to 9 subjects at each dose; 7 daily injections of Nutropin AQ, a daily, FDA-approved hGH product, at a dose of 2.4 mg of hGH, administered to 9 subjects; Each regimen was administered to patients as a subcutaneous injection.
Safety Results	ALTU-238 was generally well tolerated. There were no serious adverse events reported in the clinical trial, and the percentage of subjects who experienced adverse events was comparable among treatment groups. Subjects across all treatment groups, including subjects receiving Nutropin AQ, experienced injection site reactions, the most common of which were redness, hardening of the skin and swelling.
Clinical Activity Results	The Phase Ic pharmacokinetic and pharmacodynamic data is consistent with prior ALTU-238 clinical studies that supported an ALTU-238 once-per-week dosing regimen. The Phase 1c trial results also confirm that the ALTU-238 material, produced at the current increased manufacturing scale, performs similar to the material used in previous ALTU-238 studies.

Phase II Clinical Trial

In our Phase II clinical trial, we evaluated ALTU-238 in adults with growth hormone deficiency. The primary objective of the trial was to determine the safety and tolerability of ALTU-238, as well as its pharmacokinetic and pharmacodynamic profile, when administered over a three-week period. The goal of the

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pharmacokinetic and pharmacodynamic analyses was to confirm the once weekly dosing profile of ALTU-238 in growth hormone deficient adults. The following is a summary of our Phase II clinical trial:

ALTU-238 Phase II Clinical Trial Summary

Title	A Phase II, Multi-Center, Multi-Dose, Randomized, Open-Label, Parallel Group Study of Extended Release Crystalline Formulation of Recombinant Human Growth Hormone
Design	Growth hormone deficient men and women between the ages of 16 and 60 were randomized to receive either 5.6 mg of ALTU-238 or 11.2 mg of ALTU-238 administered in three weekly subcutaneous injections. Enrollment for the study was planned for a minimum of 12 patients with a maximum of 20 patients, including at least 4 patients in the 5.6 mg dose group and at least 6 patients in the 11.2 mg dose group. A total of 13 patients were enrolled and analyzed for safety (6 patients in the 5.6 mg group and 7 patients in the 11.2 mg group); and 11 of these patients were analyzed for the pharmacokinetics and pharmacodynamics of ALTU-238 at the end of the first week, and 10 of these patients were analyzed for the pharmacokinetics and pharmacodynamics of ALTU-238 at the end of the third week. The patients who were enrolled but not analyzed were disqualified due to documentation issues.
Administration	For each dose level, three injections of ALTU-238 were administered as subcutaneous injections one week apart.
Safety Results	ALTU-238 was generally well tolerated. There were no serious adverse events, and no patients were discontinued due to an adverse event. The majority of adverse events were considered mild or moderate in severity. There was no apparent dose-related difference between the treatment groups for the overall reporting of adverse events. Mild to moderate injection site reactions were common. We also observed changes in serum insulin and glucose, which were expected following administration of growth hormone.
Clinical Activity Results	ALTU-238, administered through a subcutaneous injection, produced hGH and IGF-1 concentrations in the blood that support a once-per-week dosing regimen. A dose response was observed for both the maximum concentration and the total concentration for hGH and IGF-1 in the blood between the 5.6 mg and 11.2 mg dose levels. As a result, we believe the dose to patients can be adjusted to achieve desired blood levels of either hGH or IGF-1. In addition, the IGF-1 profiles of the patients were reproducible following 3 weekly injections and suggest that IGF-1 concentration levels can be maintained within the normal range following repeated weekly dosing with ALTU-238.

Future Clinical Development

We have met with the FDA and EMEA to discuss the results of our Phase I and II clinical trials and future clinical development of ALTU-238 in growth hormone deficient adult and pediatric patients. After the completion of our Phase II pediatric trial discussed below, we plan to advance ALTU-238 into a Phase III clinical trial in growth hormone deficient children, as well as a Phase III clinical trial in growth hormone deficient adults.

ALTU-238 Phase II Clinical Trial in Growth Hormone Deficient Pediatric Patients

The ALTU-238 Phase II clinical trial in growth hormone deficient pediatric patients, which we plan to initiate in March 2009, is a 12-month, Phase II, randomized, open-label, multi-center, dose-ranging, parallel group study examining weekly injections of three dose levels of ALTU-238 and daily injections of one dose level of Nutropin AQ in prepubertal, rhGH-naïve children with growth hormone deficiency. The primary

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efficacy analysis is the change in annualized height velocity and will be performed after 26 weeks of treatment. This study will be divided into three periods:

Screening Period (up to 4 weeks prior to Baseline): during which eligibility will be determined.

Treatment Period: during which subjects will be randomized to one of four treatment groups and receive either weekly injections of one of three dose levels of ALTU-238 or daily injections of one dose level of Nutropin AQ for 52 weeks.

Follow-up Period (2 weeks following the End-of-Treatment visit): during which a final safety assessment will be conducted.

This study will be conducted in the target population of children with growth hormone deficiency. Subjects determined to be eligible for this study, based on screening results, will receive baseline assessments and be randomized to one of four treatment arms in a 1:1:1:1 ratio stratified by age and height standard deviation score (SDS, z-score). Only prepubertal children will be included due to the confounding effect of the pubertal growth spurt on the primary endpoint of annualized height velocity. The dosage range for ALTU-238 was selected to encompass the likely optimal dose to be used in a pivotal Phase III study. The dosage for the Nutropin AQ group is the recognized dose for the current standard of care in prepubertal children with growth hormone deficiency.

An interim efficacy analysis and the main pharmacokinetic and pharmacodynamic analysis will be performed after 14 weeks of treatment to assist in planning for a Phase III study. The primary efficacy analysis will be performed after 26 weeks of treatment, a duration which was selected to provide annualized height velocity data for use in designing a Phase III study. The entire treatment duration of 52 weeks was selected to provide definitive first year height velocity data (the primary Phase III endpoint) and other efficacy data, as well as long-term safety data.

ALTU-237 for Treatment of Hyperoxalurias and Kidney Stones

ALTU-237 is an orally-administered crystalline formulation of an oxalate-degrading enzyme which we have designed for the treatment of hyperoxalurias including primary hyperoxaluria, enteric hyperoxaluria and kidney stones in individuals with a risk or history of recurrent kidney stones. Currently, there are limited effective pharmacological treatments for primary hyperoxaluria, enteric hyperoxaluria or recurrent kidney stones.

Hyperoxalurias are a series of conditions where too much oxalate is present in the body resulting in an increased risk of kidney stones and, in rare instances, crystal formations in other organs. Increased oxalate in the body can result from eating foods that are high in oxalate, over-absorption of oxalate from the intestinal tract, and abnormalities of oxalate production by the body. Oxalate is a natural end-product of metabolism, does not appear to be needed for any human body process and is normally more than 90% excreted by the kidney. Since calcium is also continuously excreted by the kidney into the urine, oxalate can combine with calcium, causing formations of calcium-oxalate crystals which can grow into a kidney stone. In preclinical studies using rodent models, ALTU-237, delivered orally, demonstrated an ability to reduce oxalate levels in urine. We believe that reducing oxalate levels in urine may be indicative of a reduction of oxalate in the body and therefore may result in a decrease in kidney stones.

Over-absorption of oxalate from the intestinal tract, or enteric hyperoxaluria, is often associated with intestinal diseases such as inflammatory bowel disease and cystic fibrosis, or may occur in patients following gastric bypass surgery.

Primary hyperoxaluria is a rare, inherited and, if left untreated, fatal metabolic disease that results in the accumulation of oxalate in the body. Although there are variations in the disease, primary hyperoxaluria is characterized by the

shortage of an enzyme in the liver, which results in excess levels of oxalate production in the body. Based on prevalence data from an industry article, we estimate that between 1-in-60,000 and 1-in-120,000 children in North America and Europe are born with primary hyperoxaluria.

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According to the National Kidney Foundation, kidney stone disease is a common disorder of the urinary tract affecting approximately 20 million Americans. According to Disease Management, between 70% and 75% of kidney stones are composed of calcium oxalate crystals and up to 50% of patients who do not follow recommended guidelines will suffer from a repeated kidney stone incident within five years of their initial incident. According to the National Kidney and Urologic Diseases Information Clearinghouse, in 2000, kidney stones led to approximately 600,000 emergency room visits.

Preclinical Results

In a series of preclinical studies using rodent models, ALTU-237, delivered orally, demonstrated an ability to reduce oxalate levels in urine. One such study was designed to measure the impact of ALTU-237 on the reduction of hyperoxaluria in a genetic mouse model for primary hyperoxaluria. In this study, the mice were further challenged with ethylene glycol to mimic the human disease, which involves nephrocalcinosis, renal failure and potentially death. The four week study included 44 mice that received one of the following treatment regimens:

5mg, 25mg, or 80mg of ALTU-237 was orally administered to 11 mice at each dose

11 mice received no treatment and served as a control group

In the study, ALTU-237 therapy resulted in a sustained reduction of urinary oxalate levels as evidenced by a reduction in urinary oxalate of 30 to 50 percent in all treatment groups as compared to the control group. In addition, a reduction in nephrocalcinosis and an increase in survival rate were observed in mice in the two lower dose groups and there was no nephrocalcinosis, renal failure or death in any mouse in the high dose group.

Phase I Clinical Trial

In the second quarter of 2008, we reported results from a Phase I clinical trial of ALTU-237. The primary objective of this trial was to determine the safety and tolerability of escalating dose levels of ALTU-237 in normal healthy adults.

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The study enrolled 58 normal healthy adults that were randomized into four cohorts. During a baseline period, subjects in each cohort consumed a low oxalate, high calcium diet to establish a consistent, low urinary oxalate baseline level prior to treatment. After the baseline period, subjects were randomized to receive either ALTU-237 or placebo during a seven day, double blind treatment period. During this treatment period, subjects consumed a high oxalate, low calcium diet. Safety assessments were performed throughout the study. Results of this trial are summarized in the table below.

ALTU-237 Phase I Clinical Trial Summary

Title	A Phase I, Single-Center, Double-blind, Placebo-Controlled, Dose Escalating Study Evaluating the Safety and Clinical Activity of ALTU-237 in Normal Healthy Adults on a Controlled, High Oxalate Diet
Design	Double-blind, dose escalation, placebo-controlled study to evaluate the safety and clinical activity of ALTU-237 in normal, healthy adult males and females consuming a controlled, high oxalate diet. Four groups of up to 32 subjects were enrolled in the low oxalate diet period. Up to sixteen of these subjects were randomized to receive either escalating doses of ALTU-237 of approximately 900, 3600, 10,800, and 18,000 units/day or placebo. The remaining subjects were alternates. ALTU-237 (and placebo) were administered orally as capsules with meals three times a day. This study was conducted on an inpatient basis. During a five-day baseline period, each cohort consumed a low oxalate, high calcium diet to establish a consistent, low urinary oxalate baseline level prior to treatment. Subjects were then be randomized at a 3:1 ratio (three ALTU-237 subjects to every one placebo subject) to receive either ALTU-237 or placebo during a seven-day, double-blind treatment period. During this double-blind treatment period, subjects consumed a high oxalate, low calcium diet. The treatment period lasted seven days.
Administration	ALTU-237 was administered orally with meals during the treatment period.
Safety Results	All doses were well-tolerated and no severe adverse events were reported.

The ALTU-237 development program is on hold until we are able to secure additional funding.

Our Preclinical Research and Development Programs

We have a pipeline of preclinical product candidates that are designed to either substitute protein that is in short supply in the body or degrade toxic metabolites in the gut and remove them from the blood stream. We have designed all of these product candidates for oral delivery to address areas of unmet need in gastrointestinal and metabolic disorders, including an enzyme that degrades phenylalanine for the treatment of phenylketonuria and an enzyme that degrades urate for the treatment of gout. We believe that our proprietary, crystallized formulations of these product candidates will represent novel or improved therapies for the treatment of these disorders. Our two most advanced preclinical product candidates are described below.

ALTU-236 for Treatment of Hyperphenylalanemia

ALTU-236 is an orally-administered enzyme replacement therapy product candidate designed to reduce the long-term effects associated with excess levels of phenylalanine, also known as hyperphenylalanemia. According to the National Institutes of Health, phenylketonuria, or PKU, which is the most severe form of hyperphenylalanemia, affects approximately 1-in-15,000 newborns in the United States. PKU is a rare, inherited, metabolic disorder that results from an enzyme deficiency that causes the accumulation of the amino acid phenylalanine in the body. If left untreated, PKU can result in mental retardation, swelling of the brain, delayed speech, seizures and behavior abnormalities. Virtually all newborns in the United States and in many other countries are screened prior to leaving the hospital for

PKU. There is currently one approved drug to treat certain patients with PKU. However, the majority of patients suffering from PKU and hyperphenylalanemia are currently treated with a phenylalanine restricted diet. This diet is expensive and difficult to maintain and does not avoid many of the long-term effects of PKU.

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ALTU-242 for Treatment of Gout

ALTU-242 is an orally-administered enzyme product candidate designed to reduce the long-term effects associated with excess levels of urate, the cause of gout. Excess levels of urate can precipitate and form crystals in joints causing a painful erosive arthritis commonly referred to as gout. Gout is a common disorder that affects at least 1% of the population in Western countries and is the most common inflammatory joint disease in men over 40 years of age. Data suggest that there are more than 1.6 million diagnoses of gout in the United States annually.

The ALTU-236 and ALTU-242 development programs are on hold until we are able to secure additional funding.

Trizytek for Exocrine Pancreatic Insufficiency

Pancreatic insufficiency is a deficiency of the digestive enzymes normally produced by the pancreas and can result from a number of disease conditions, including cystic fibrosis, chronic pancreatitis and pancreatic cancer. Patients with exocrine pancreatic insufficiency are currently treated with enzyme replacement products containing enzymes derived from pig pancreases. Trizytek is a non-porcine pancreatic enzyme replacement therapy for the treatment of malabsorption due to exocrine pancreatic insufficiency consisting of three APIs; lipase, protease and amylase, which aid in the digestion of fat, proteins and carbohydrates.

On January 26, 2009, we announced a strategic realignment and the discontinuation of our activities in support of Trizytek. On February 20, 2009, CFFTI and we entered into a series of agreements to terminate our strategic alliance agreement. As part of these agreements, we will assist CFFTI with a transition of our on-going development and regulatory activities and clinical trials through March 27, 2009, after which CFFTI will be responsible for future development activities.

We have completed five clinical trials of Trizytek, four of which were in cystic fibrosis patients and one of which was in healthy volunteers. The following table summarizes the clinical trials of Trizytek that we have completed to date:

Trial	Number of Subjects	Primary Study Objective
Phase Ia	20 healthy volunteers	Safety and tolerability over 7 days of dosing
Phase Ib	23 cystic fibrosis patients	Safety, tolerability and clinical activity over 3 days of dosing
Phase Ic	8 cystic fibrosis patients	Safety, tolerability and clinical activity over 14 days of dosing
Phase II	129 cystic fibrosis patients	Safety, tolerability and efficacy over 28 days of dosing
Phase III	163 cystic fibrosis patients	Safety, tolerability and efficacy over approximately 2 months of dosing

Our clinical trials with cystic fibrosis patients assessed a number of different measures, or endpoints, of digestion and absorption. We assessed fat absorption by measuring a patient s fat intake over a specified period of time and comparing that to the amount of fat in their stool during the same period. This comparison enabled us to calculate the amount of fat a patient absorbed, using a metric known as the coefficient of fat absorption, or CFA. The same process was applied to determine protein absorption, using a metric called the coefficient of nitrogen absorption, or CNA. We measured carbohydrate absorption by analyzing a patient s blood glucose levels after a starch meal, using a test we refer to as the starch challenge test. In our Phase Ib, Phase II and Phase III clinical trials, we also measured the number and weight of the patients stools.

Phase III Clinical Trial in Cystic Fibrosis Patients

We designed our pivotal Phase III clinical trial of Trizytek to be a multicenter, randomized, double-blind, placebo-controlled clinical study to determine, as the primary endpoint, the efficacy of Trizytek in the treatment of fat malabsorption in cystic fibrosis patients with exocrine pancreatic insufficiency through measurement of CFA. The trial also included secondary efficacy endpoints, including the evaluation of

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Trizytek in the treatment of protein absorption through measurement of CNA and carbohydrate absorption through the use of the starch challenge test. We also assessed the ability of Trizytek to decrease the weight and frequency of stools in patients. In the trial, we also evaluated the safety and tolerability of Trizytek over an approximate two month dosing period.

At the beginning of the Phase III trial, we obtained baseline measurements of fat, protein and carbohydrate absorption during a hospital stay of up to one week. After the baseline period was complete, patients were released from the hospital and placed on open-label therapy with Trizytek. All of the patients in the trial had one capsule of Trizytek with each meal or snack for approximately four weeks. The selected dose of lipase, protease and amylase was consistent with the middle dose in our Phase II clinical trial. After this four-week period, patients returned to the hospital for up to one week for a second in-hospital stay. During this hospital stay, patients were randomized on a one-to-one basis, and stratified based on whether their baseline measurements of CFA place them in the subgroup of patients having absorption of less than 40% or the subgroup of patients having absorption of greater than or equal to 40% but not more than 80% to receive either Trizytek or placebo. Fat, protein and carbohydrate absorption were measured using the same process that was used to establish the baseline level during the first in-hospital stay. A comparison of each patient s measurements during the two in-hospital periods was performed in the analysis of the endpoints for the trial. After the second in-hospital stay, patients returned to open-label therapy with Trizytek for one week to complete the study. We reported the results of this trial in the third quarter of 2008.

Long-Term Safety Studies

Before our strategic realignment, we initiated two clinical studies evaluating the long-term safety of Trizytek. One study is being conducted in cystic fibrosis patients and one study is being conducted in chronic pancreatitis patients with exocrine pancreatic insufficiency. The studies are designed to evaluate the safety of Trizytek following one year of open-label treatment in order to provide the necessary six-month and 12-month exposure data for approval of a new drug application, or NDA. We enrolled a total of approximately 256 patients with pancreatic insufficiency into the two studies, which included some of the eligible patients from our Phase III efficacy trial of Trizytek. CFFTI has assumed responsibility for the safety study in cystic fibrosis patients and we have discontinued the study in chronic pancreatitis patients.

Phase III Efficacy Results

The trial met its primary efficacy endpoint with statistical significance. In cystic fibrosis patients with exocrine pancreatic insufficiency, Trizytek demonstrated a statistically significant improvement of fat absorption over placebo through the measurement of the CFA. The primary efficacy analysis was an intent to treat, or ITT, analysis in the sub-group of patients with severe malabsorption (patients with baseline CFAs below 40). In addition, data were analyzed for the overall group, which included all patients with baseline CFA below 80.

Primary Endpoint CFA Results

	Trizytek		Placebo			
Baseline CFA Group	**Baseline**	**Improvement from Baseline**	**Baseline**	**Improvement from Baseline**	**Mean Difference Between Groups**	**P-Value**
<40	30.0	20.2 points or 79.6%	28.1	5.1 points or 24.4%	15.1	0.001

Overall	46.9	11.3 points or 35.8%	49.5	0.2 points or 4.3%	10.6	<0.001

Of the 138 patients in the ITT analysis, 68 patients were at cystic fibrosis centers within the United States and 70 patients were at sites outside of the United States. A strong country effect was seen that impacted the overall outcome. For U.S. patients in the Trizytek CFA<40 group, there was an improvement in the mean CFA of 28.4 (115% change from baseline). In the placebo CFA<40 group, there was an increase in mean CFA of 3.4 (23% change from baseline). The mean difference between groups for the change in CFA was 25.1 (p =0.001). In contrast, the mean difference in the CFA<40 group in countries outside of the U.S. was 5.0.

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For U.S. patients in the overall group who received Trizytek, there was an improvement in the mean CFA of 15.7 (48% change from baseline). For U.S. patients on placebo in the overall group, there was a decrease in the mean CFA of -2.1 (1% change from baseline). The mean difference between groups for the change in CFA was 17.5 (p=<0.001). In contrast, the mean difference in the overall group in countries outside of the U.S. was 4.3. The U.S. results are summarized in the table below.

Primary Endpoint CFA Results US Sites

	Trizytek		Placebo			
Baseline CFA Group	**Baseline**	**Improvement from Baseline**	**Baseline**	**Improvement from Baseline**	**Mean Difference Between Groups**	**P-Value**
<40	27.0	28.4 points or 115.4%	23.6	3.4 points or 22.6%	25.1	0.001
Overall	46.3	15.7 points or 48.3%	43.7	−2.1 points or 0.7%	17.5	<0.001

The trial also evaluated secondary efficacy endpoints. Patients treated with Trizytek had a statistically significant improvement in CNA compared to placebo (p =<0.001). The Phase III CNA results paralleled the Phase III CFA results. There was not a statistically significant improvement in carbohydrate absorption compared to placebo on the starch challenge test. Importantly, there was a significant decrease in stool weight in Trizytek treated patients compared to placebo (p=0.001). Trizytek was well-tolerated and had a favorable safety profile in the trial. There were no serious adverse events attributed to the Trizytek treatment.

Our Protein Crystallization Technology and Approach

Historically, scientists have crystallized proteins primarily for use in x-ray crystallography to examine the structure of proteins in small batches. In contrast, we are using our technology to crystallize proteins in significantly larger amounts for use as therapeutic drugs. This requires the crystallization process to be both reproducible and scalable, and our technology is designed to enable large scale crystallization with batch-to-batch consistency.

Crystallized proteins are more stable, pure and concentrated than proteins in solution. For example, one protein crystal may contain several billion molecules of the underlying protein. We believe that these characteristics will enable improved storage and delivery, permitting delivery of the protein molecules with fewer capsules or smaller injection volumes.

Once a protein is in the crystallized state, we formulate it for either oral or injectable delivery. For our product candidates that will be delivered orally, we use our crystallization technology to deliver proteins to the gastrointestinal tract, where they can exert their therapeutic effect locally. In situations where we need to confer a higher level of stability to a protein, such as in the lipase component of Trizytek, we cross-link protein molecules in crystals together using multi-functional cross-linking agents. For our product candidates that are injected, we use our crystallization technology to develop highly concentrated and stable proteins that can be formulated for extended release.

Our approach to developing therapeutic product candidates using crystallized proteins is comprised of the following general elements:

Establish initial crystallization conditions. Once we choose a target protein, we rapidly screen hundreds of crystallization conditions both manually and using robotics. We define the conditions under which a soluble protein could crystallize, including protein concentration, pH and temperature of crystallization.

Identify key crystallization conditions and initial crystallization scale up. After we identify the initial conditions, we focus on the critical crystallization conditions to define a robust and reproducible crystallization process. We then scale the process from single drops, to microliter scale, to milliliter scale, and finally, to liter scale.

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Select crystallization process and crystal. If there is more than one successful crystallization process and resulting crystals, we use our target product profile to choose the best protein crystal for the given application based on crystal size, shape and other characteristics.

We apply our proprietary protein crystallization technology to existing, well understood proteins in the development of our product candidates. We believe our technology is broadly applicable to all classes of proteins, including enzymes, hormones, antibodies, cytokines and peptides. To date, we have crystallized more than 70 proteins for evaluation in our product candidates and preclinical research and development programs.

Collaborations

Cystic Fibrosis Foundation Therapeutics, Inc.

In February 2001, we entered into a strategic alliance agreement with CFFTI, an affiliate of the Cystic Fibrosis Foundation. Under this agreement, which was amended in 2001 and 2003, we and CFFTI agreed to collaborate for the development of Trizytek and specified derivatives of Trizytek in North America for the treatment of malabsorption due to exocrine pancreatic insufficiency in patients with cystic fibrosis and other indications. The agreement, in general terms, provided us with funding from CFFTI for a portion of the development costs of Trizytek upon the achievement of specified development and regulatory milestones, up to a total of $25.0 million, in return for specified payment obligations described below and our obligation to use commercially reasonable efforts to develop and bring Trizytek to market in North America for the treatment of malabsorption due to exocrine pancreatic insufficiency in patients with cystic fibrosis and other indications. CFFTI also agreed to provide us with reasonable access to its network of medical providers, patients, researchers and others involved in the care and treatment of cystic fibrosis patients, and to use reasonable efforts to promote the involvement of these parties in the development of Trizytek. In connection with the agreement, we also issued CFFTI warrants to purchase a total of 261,664 shares of common stock at an exercise price of $0.02 per share. As of December 31, 2008, we had received a total of $18.4 million of the $25.0 million available under the agreement.

Under the terms of the agreement, we granted CFFTI an exclusive license under our intellectual property rights covering Trizytek and specified derivatives for use in all applications and indications in North America, and CFFTI granted us back an exclusive sublicense of the same scope, including the right to grant further sublicenses.

To conserve capital resources, we discontinued our Trizytek program activities in January 2009. On February 20, 2009, CFFTI and we entered into the Letter Agreement and the License Agreement terminating our strategic alliance agreement. Under the terms of the License Agreement, we assigned the Trizytek trademark and certain patent rights to CFFTI and granted CFFTI an exclusive, worldwide, royalty-bearing license to use certain other intellectual property owned or controlled by us to develop, manufacture and commercialize any product using, in any combination, the three APIs which comprise Trizytek. In these agreements, we also agreed to assist CFFTI with a transition of our on-going development and regulatory activities and clinical trials through March 27, 2009, after which CFFTI will be responsible for future development activities. In exchange, CFFTI agreed to release us from all obligations and liabilities resulting from the original strategic alliance agreement, and to pay us a percentage of any proceeds CFFTI realizes associated with respect to any rights licensed or assigned to CFFTI under the License Agreement.

Dr. Falk Pharma GmbH

In December 2002, we entered into a development, commercialization and marketing agreement with Dr. Falk Pharma GmbH, or Dr. Falk, for the development by us of Trizytek and the commercialization by Dr. Falk of Trizytek, if approved, in Europe, the countries of the former Soviet Union, Israel and Egypt. Under the agreement, we granted

Dr. Falk an exclusive, sublicensable license under specified patents that cover Trizytek to commercialize Trizytek for the treatment of symptoms caused by exocrine pancreatic insufficiency.

In June 2007, we reacquired from Dr. Falk the development and commercialization rights to Trizytek and ended the development and commercialization collaboration in Europe and countries of the former Soviet

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Union, Israel and Egypt. Dr. Falk and we had differing views regarding the optimal development and commercialization path for Trizytek and ultimately concluded that acquisition of the development and commercialization rights by us would be in the best interest of both parties.

Under the termination agreement, we regained control of all of the assets created in the collaboration. In addition, Dr. Falk has agreed to transfer the July 2004 Orphan Medicinal Product Designation granted to Dr. Falk by the European Agency for the Evaluation of Medicinal Products. In exchange, we agreed to pay Dr. Falk 12.0 million over three years. As of the termination of the collaboration agreement, we had received a total of 11 million in milestone payments from Dr. Falk.

Manufacturing

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of any of our product candidates. We currently have no plans to build our own clinical- or commercial-scale manufacturing capabilities, and we expect for the foreseeable future to rely on contract manufacturers for both clinical and commercial supplies of our products. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee the relationships with our contract manufacturers.

ALTU-238

We entered into a drug production and clinical supply agreement with Althea Technologies, Inc., or Althea, in August 2006. Under this agreement, Althea agreed to modify an existing production facility, and test and validate its manufacturing operations for the production of ALTU-238. Althea completed these activities and produced ALTU-238 for the Phase Ic trial and Phase II pediatric trial. The agreement terminates following the production of a defined number of manufacturing runs of ALTU-238, from which we intend to supply planned clinical trials. The agreement is subject to early termination by either party in the event of an uncured material breach by or bankruptcy of the other party. Althea s liability to us for any breach of the agreement is limited to an obligation to replace those products which do not conform to requirements.

In addition, we and Althea have agreed to negotiate an agreement under which Althea will provide ALTU-238 for commercial supply. Alternatively, if within one year after the termination or expiration of the agreement, other than a termination due to Althea s uncured breach, we enter into an agreement with a third party to provide commercial supply of ALTU-238, we must make a one-time payment to Althea.

In July 2008, we signed a long-term agreement to purchase recombinant human growth hormone, or hGH, for ALTU-238 for development and commercialization. The agreement was signed with Sandoz GmbH, a Novartis company. Sandoz supplied hGH for Altus completed Phase Ic clinical trial in healthy adults and the Phase 2 clinical trial in adults with growth hormone deficiency. In connection with this agreement, we are required to provide Sandoz with a forecast of our hGH requirements for the next three calendar years. Under the terms of the agreement, we are obligated to purchase all of the hGH forecasted for the first calendar year and 50% of the hGH forecasted for the second calendar year. We are not obligated to purchase any of the hGH forecasted for the third calendar year. As of December 31, 2008 our minimum contractual obligation to Sandoz under the terms of the agreement was $4.8 million and $2.4 million for 2009 and 2010, respectively, based on the foreign currency exchange rate at December 31, 2008.

Trizytek

Amano

Amano Enzyme, Inc., or Amano, manufactured the clinical supplies of the crystallized and cross-linked lipase, the crystallized protease, and the amylase enzymes that comprise the APIs for Trizytek.

Amano has built a plant near Nagoya, Japan to produce the enzymes for Trizytek in large-scale batches using microbial fermentation. The plant has not been inspected or approved by the FDA, EMEA or the Japanese Ministry of Health, Labour and Welfare. Amano supplied the APIs for Trizytek for the non-clinical and clinical trials to date. We used a third party, Patheon Inc., to perform fill, finish and packaging services for Trizytek.

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Under the terms of our original agreement with Amano, each party contributed technology used for the production of the APIs in Trizytek. Each party owns intellectual property created solely by it, and jointly owns any intellectual property created jointly. In connection with our entry into the agreement with Lonza Ltd., or Lonza, described below, Amano has agreed to transfer technology relating to Trizytek to Lonza. On December 20, 2007, we and Amano entered into an additional agreement. Under this agreement, Amano granted to us a royalty-bearing license to technology owned by Amano to manufacture proteins in bulk form for use by us in preparing the supply of Trizytek for clinical and commercial purposes. We sublicensed this technology to CFFTI as part of the License Agreement we entered into with CFFTI on February 20, 2009.

Lonza

In November 2006, we entered into a six-year manufacturing and supply agreement with Lonza for the manufacturing and supply of commercial quantities of the crystallized and cross-linked lipase, the crystallized protease and the amylase enzymes that comprise the APIs for Trizytek. This agreement provides for the transfer of manufacturing technology to Lonza, the installation of specialized manufacturing equipment for the manufacturing process, the validation of the manufacturing facility, and the supply of these enzymes for commercial purposes. We planned to continue to use a third party to perform fill, finish and packaging services for the commercial supply of Trizytek.

Under the agreement, Lonza agreed to manufacture the APIs in accordance with defined specifications and applicable cGMP and international regulatory requirements. Subject to customary notice, reservation and forecasting procedures, Lonza agreed to reserve capacity at its facility for supply of the APIs that we believed would meet our needs for APIs for use in the commercial launch of Trizytek. We were to provide binding purchase orders to Lonza annually, and we have committed to purchase a specified number of batches, and a specified percentage of our requirements, from Lonza during specified periods. As of December 31, 2008, our total commitment to Lonza related to our binding purchase order is approximately $4.5 million. However, if Lonza was unable to meet specified production and delivery requirements, we would have the right to reduce payments or engage third-party suppliers, depending on the extent of the shortfall. If Lonza built or acquired more capacity for the manufacture of the APIs, we agreed to use commercially reasonable efforts to purchase additional batches of the APIs from Lonza.

The agreement is subject to automatic renewal at the expiration of its six-year term for successive two year terms unless we provide Lonza with notice prior to expiration of each term of our decision to terminate. Each party has the right to terminate the agreement upon the occurrence of an uncured material breach or the bankruptcy of the other party. We have the right to terminate the agreement in the event that we cease development or commercialization of Trizytek due to toxicity, efficacy or other technical or business considerations, in which case we must make a payment to Lonza if we have not already purchased from Lonza a specified value of APIs. Lonza has the right to terminate the agreement in the event that we do not order a defined quantity of enzymes for delivery from the capacity reserved for us by Lonza for the production of Trizytek. Lonza also has the right to terminate the agreement if we fail to arrange for the delivery of certain materials and technology that are necessary for Lonza to manufacture the enzymes in accordance with the specifications for production.

As a result of our discontinuation of the Trizytek program, we are evaluating our options regarding the agreement with Lonza.

Competition

Our major competitors are pharmaceutical and biotechnology companies in the United States and abroad that are actively engaged in the discovery, development and commercialization of products to treat gastrointestinal and metabolic disorders. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of the entities developing and marketing potentially competing products have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing than we do. These entities also compete with us in

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recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to our programs.

Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected because in some cases insurers and other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers.

If our clinical-stage product candidates are approved for commercial sale, they will compete with currently marketed drugs and potentially with drug candidates currently in development for the same indications, including the following:

ALTU-238. If approved, ALTU-238, the product candidate we are developing as a once-weekly treatment for hGH deficiency and related disorders, will compete with approved hGH therapies from companies such as BioPartners, Eli Lilly, Genentech, Novo Nordisk, Pfizer, Sandoz, Serono and Teva Pharmaceutical Industries. In addition, we understand that ALTU-238 may compete with product candidates in clinical development from some of these companies and from others, including LG Life Sciences, which is developing a long-acting hGH therapy based on an encapsulated microparticle technology, and Ambrx Inc., which is also developing a long-acting hGH therapy in conjunction with Serono.

ALTU-237. If approved, ALTU-237, the product candidate we are developing for the treatment of hyperoxalurias, may compete with products in development at companies such as Amsterdam Molecular Therapeutics, Medix, NephroGenex, and OxThera.

We believe that the key differentiating elements affecting the success of our product candidates are likely to be their convenience of use and efficacy and safety profile compared to other therapies.

Intellectual Property

We actively seek patent protection for the proprietary technology that we consider important to our business, including compounds, compositions and formulations, their methods of use and processes for their manufacture. In addition to seeking patent protection in the United States, we generally file patent applications in Canada, Europe, Japan and additional countries on a selective basis in order to further protect the inventions that we consider important to the development of our business worldwide. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing our proprietary rights.

Our patent portfolio includes patents and patent applications with claims relating to protein crystals, both cross-linked and non-cross-linked, as well as compositions of specific protein crystals, such as lipase and hGH, and methods of making and using these compositions. In addition, we currently have patent applications relating to compositions and formulations containing both cross-linked and non-cross-linked protein crystals and patent applications relating to some of our later stage pipeline products.

As of December 31, 2008, our patent estate on a worldwide basis includes 14 patents issued in the United States and 43 issued in other countries, many of which are foreign counterparts of our United States patents, as well as more than 100 pending patent applications, with claims covering all of our product candidates.

We have pending United States patent applications relating to ALTU-238, which if issued as patents, would expire between 2019 and 2027, and include claims relating to hGH crystals with an extended release profile and methods of treating hGH deficiency associated disorders using such hGH crystals. We also have pending foreign patent applications relating to ALTU-238, which if issued as patents, would expire between 2019 and 2027.

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Five of our United States patents, which have claims covering cross-linked protein or enzyme crystals and methods of using those crystals in enzyme and oral protein therapy and methods of making cross-linked crystals with controlled dissolution properties, also relate to ALTU-237. These patents expire between 2014 and 2017. Additionally, we have two pending United States patent applications relating to ALTU-237, which if issued as patents, would expire between 2026 and 2027. Some of these applications include claims covering specific oxalate degrading enzyme formulations, methods of making formulations, and methods of treatment using these formulations.

Four of our issued United States patents, expiring between 2014 and 2016, relate to Trizytek and have claims covering cross-linked protein crystals, cross-linked enzyme crystals and methods of using those crystals in enzyme and oral protein therapy. We also have five pending United States patent applications relating to Trizytek, which if issued as patents, would expire between 2017 and 2025. Some of these applications include claims covering a combination of lipase, protease and amylase in specific formulations and methods of treatment using these formulations. We also have 38 issued foreign patents, expiring between 2011 and 2021, relating to Trizytek and pending foreign patent applications, which if issued as patents, would expire between 2011 and 2025. Our U.S. patents and patent applications and foreign counterparts solely relating to lipase, amylase and protease, including Trizytek, have been assigned to CFFTI and certain other patents have been licensed to CFFTI.

Our patent estate includes patent applications relating to some of our other product candidates. These patent applications, assuming they issue as patents, would expire between 2021 and 2024. We also have eight other issued United States patents and various foreign counterparts that relate to cross-linked protein crystal biosensors, methods of using cross-linked crystals of thermolysin as a catalyst, stabilized protein crystals, protein crystal formulations as catalysts in organic solvents and cross-linked glycoprotein crystals.

We hold an exclusive, royalty-free, fully-paid license from Vertex to patents relating to cross-linked enzyme crystals, including the four issued United States patents relating to Trizytek and ALTU-237 and two other issued United States patents relating to biosensors and thermolysin, as well as to a number of corresponding foreign patents and patent applications and know-how, including improvements developed by Vertex or its collaborators through February 2004. Under this license, Vertex retains non-exclusive rights to use the licensed Vertex patents and know-how to develop and commercialize small molecule drugs for human or animal therapeutic uses. We also granted to Vertex a non-exclusive, royalty-free, fully-paid license, under our patents and know-how with respect to cross-linked protein crystals that we have acquired, developed or licensed through February 2004, for Vertex s use in small molecule drug development and commercialization for human or animal therapeutic uses. The licenses with respect to patents, unless otherwise terminated earlier for cause, terminate on a country-by-country basis upon the expiration of each patent covered by the license.

We also have rights to specified technology developed by Amano under our cooperative development agreement with Amano, as described above under the section entitled Manufacturing.

Individual patents extend for varying periods depending on the effective date of filing of the patent application or the date of patent issuance, and the legal term of the patents in the countries in which they are obtained. Generally, patents issued in the United States are effective for:

- the longer of 17 years from the issue date or 20 years from the earliest effective filing date, if the patent application was filed prior to June 8, 1995; and
- 20 years from the earliest effective filing date, if the patent application was filed on or after June 8, 1995.

The term of foreign patents varies in accordance with provisions of applicable local law, but typically is 20 years from the earliest effective filing date. In addition, in some instances, a patent term in the United States and outside of the

United States can be extended to recapture a portion of the term effectively lost as a result of the health authority regulatory review period. These extensions, which may be as long as five years, are directed to the approved product and its approved indications. We intend to seek such extensions as appropriate.

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The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications that are licensed to us will result in the issuance of any patents or if issued will assist our business. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented. This could limit our ability to stop competitors from marketing related products and reduce the length of term of patent protection that we may have for our products. In addition, the rights granted under any of our issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Our competitors may develop similar technologies, duplicate any technology developed by us, or use their patent rights to block us from taking the full advantage of the market. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that a related patent may remain in force for a short period following commercialization, thereby reducing the advantage of the patent to our business and products.

In addition to patents, we may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect the trade secrets in our proprietary technology and processes, in part, by entering into confidentiality agreements with commercial partners, collaborators, employees, consultants, scientific advisors and other contractors and into invention assignment agreements with our employees and some of our commercial partners and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of the technologies that are developed. 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.

Many of our employees, consultants and contractors have worked for others in the biotechnology or pharmaceutical industries. We try to ensure that, in their work for us, they do not use the proprietary information or know-how of others. To the extent that our employees, consultants or contractors use proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing.

United States Government Regulation

In the United States, the information that must be submitted to the FDA in order to obtain approval to market a new drug varies depending on whether the drug is a new product whose safety and effectiveness has not previously been demonstrated in humans or a drug whose active ingredients and some other properties are the same as those of a previously approved drug. A new drug will follow the NDA route and a new biologic will follow the biologic license application, or BLA, route.

NDA and BLA Approval Processes

In the United States, the FDA regulates drugs and some biologics under the FDCA, and in the case of the remaining biologics, also under the Public Health Service Act, and implementing regulations. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include:

the FDA s refusal to approve pending applications;

license suspension or revocation;

withdrawal of an approval;

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a clinical hold;

warning letters;

product recalls;

product seizures;

total or partial suspension of production or distribution; or

injunctions, fines, civil penalties or criminal prosecution.

Any agency or judicial enforcement action could have a material adverse effect on us. The process of obtaining regulatory approvals and the subsequent substantial compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

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

completion of nonclinical laboratory tests according to good laboratory practice regulations, or GLP;

submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;

performance of adequate and well-controlled human clinical trials according to good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug for its intended use;

submission to the FDA of an NDA or BLA;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity or to meet standards designed to ensure the biologic s continued safety, purity and potency; and

FDA review and approval of the NDA or BLA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical or non-clinical testing may continue even after the IND is submitted. In addition to including the results of the preclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, specifically places the clinical trial on clinical hold. The FDA can also place a trial on clinical hold at any time after it commences. In these cases, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin or resume.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent. Further, an Institutional Review Board, or IRB, at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Each new clinical protocol must be submitted to the FDA as part of the IND. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur.

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Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

Phase I: The drug is initially introduced into healthy human subjects or patients with the disease and tested for safety, dosage tolerance, pharmacokinetics, pharmacodynamics, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

Phase II: Involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase III: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide, if appropriate, an adequate basis for product labeling.

Phase I, Phase II and Phase III testing may not be completed successfully within any specified period, if at all. The FDA or an IRB or the sponsor may suspend or terminate a clinical trial at any time for various reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk.

Concurrent with clinical trials, companies usually complete additional animal studies and must also must develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product 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 final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf-life.

The results of product development, preclinical studies and clinical studies, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, results of chemical studies and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs and BLAs submitted before it accepts them for filing. It may request additional information rather than accept an NDA or BLA for filing. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data is submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacture is cGMP-compliant to assure and preserve the product s identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product s continued safety, purity and potency. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory authorities typically takes at least several years and the actual time required may vary substantially, based upon, among other things, the

type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly procedures upon our activities. Success in early stage clinical trials does not assure success in later stage clinical trials. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or

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at all. Even if a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited which could restrict the commercial application of the products. Further, even after regulatory approval is obtained, 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. Delays in obtaining, or failures to obtain regulatory approvals for any drug candidate could substantially harm our business and cause our stock price to drop significantly. In addition, we cannot predict what adverse governmental regulations may arise from future United States or foreign governmental action.

Expedited Review and Approval

The FDA has various programs, including fast track, priority review and accelerated approval, that are intended to expedite or simplify the process for reviewing drugs and provide for approval on the basis of surrogate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that may be 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. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. Although fast track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a fast-track designated drug and expedite review of the application for a drug designated for priority review. Drugs that receive an accelerated approval may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials.

Pediatric Exclusivity

The FDA Modernization Act of 1997 included a pediatric exclusivity provision that was extended by the Best Pharmaceuticals for Children Act of 2002. Pediatric exclusivity is designed to provide an incentive to manufacturers for conducting research about the safety of their products in children. Pediatric exclusivity, if granted, provides an additional six months of market exclusivity in the United States for new or currently marketed drugs. Under Section 505A of the FDCA, six months of market exclusivity may be granted in exchange for the voluntary completion of pediatric studies in accordance with an FDA-issued Written Request. The FDA may not issue a Written Request for studies on unapproved or approved indications where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not requested or received a Written Request for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies, and submit reports of the studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles. The FDA may not issue a Written Request for such studies if we ask for one, and it may not accept the reports of the studies. The current pediatric exclusivity provision is scheduled to end on October 1, 2012, and it may not be reauthorized, or may be reauthorized in a more limited form.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. 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 require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA

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has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the drug;
- implementation of risk management plans and providing the FDA with updated safety and efficacy information;
- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- complying with certain electronic records and signature requirements; and
- complying with FDA promotion and advertising requirements.

Drug manufacturers and their subcontractors are required to register their manufacturing facilities with the FDA and some state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

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

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sale and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, we may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by biotechnology and optional for those which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessments

report each member state must decide whether to recognize approval. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

As in the United States, we may apply for designation of our products as orphan drugs for the treatment of specific indications in the European Union before the application for marketing authorization is made. Orphan drugs in the European Union enjoy economic and marketing benefits, including a 10-year market

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exclusivity period for the approved indication for the same or similar drug, unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product. For example, the EMEA has granted Trizytek orphan drug designation.

Reimbursement

Sales of biopharmaceutical products depend in significant part on the availability of coverage through third-party payment systems. We anticipate third-party payors will provide coverage and reimbursement for our products. It will be time consuming and expensive for us to seek coverage from third-party payors for newly-approved drugs, and the scope of such coverage might be more limited than the purposes for which the FDA approves the drug. Eligibility for coverage does not imply that any drug will be reimbursed in all cases or at a rate that would be sufficient to allow us to sell our products on a competitive and profitable basis. Interim payments for new drugs, if applicable, might not be sufficient to cover our costs, and such payment might not be made permanent. Reimbursement rates vary according to the use of the drug, the clinical setting in which it is used, and whether it is administered by a physician in connection with a specific service or procedure. Reimbursement rates may be based upon payments allowed for lower-cost products that are already covered; may be incorporated into unprofitable composite rates for other services; and may reflect budgetary constraints, political considerations, and imperfections in data affecting government-funded health care programs. Drug prices may be reduced by mandatory discounts or rebates imposed by third party payors. Third party payors often follow the coverage and reimbursement policies established by government-funded health care programs such as Medicare. As a result, Medicare coverage and reimbursement policies may affect the pricing and profitability of drugs whether or not Medicare beneficiaries are expected to comprise a significant portion of the patients using the drug.

The levels of revenues and profitability of biopharmaceutical companies may also be affected by the continuing efforts of government and third party payors to contain or reduce the costs of health care through various means. For example, in some foreign markets, pricing reimbursement or profitability of therapeutic and other pharmaceutical products is subject to governmental control. In Canada, this practice has led to lower priced drugs than in the United States. As a result, importation of drugs from Canada into the United States may result in reduced product revenues.

In the United States there have been, and we expect that there will continue to be, a number of federal and state proposals to implement governmental pricing reimbursement controls. The Medicare Prescription Drug and Modernization Act of 2003 imposed new requirements for the distribution and pricing of prescription drugs that may affect the marketing of our products, if we obtain FDA approval for those products. Under this law, Medicare was extended to cover a wide range of prescription drugs other than those directly administered by physicians in a hospital or medical office. Competitive regional private drug plans were authorized to establish lists of approved drugs, or formularies, and to negotiate rebates and other price control arrangements with drug companies. Proposals to allow the government to directly negotiate Medicare drug prices with drug companies, if enacted, might further constrain drug prices, leading to reduced revenues and profitability. While we cannot predict whether any future legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Employees

We believe that our success will depend greatly on our ability to identify, attract and retain capable employees. As of December 31, 2008, we had 145 employees, of whom 30 held Ph.D. or M.D. degrees. The

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realignment that we announced on January 26, 2009 included a workforce reduction of approximately 75%, primarily in functions related to the Trizytek program as well as certain general and administrative positions. After the realignment, which we expect to be completed by the end of the first half of 2009, we will have approximately 34 employees, including approximately 22 in research and development positions and approximately 12 administrative and support positions. We believe that relations with our employees are good. None of our employees is represented under a collective bargaining agreement.

Available Information

Our principal executive offices are located at 333 Wyman Street, Waltham, MA 02451, and our telephone number is (781) 373-6000. Our website address is *www.altus.com*. The information contained on, or that can be accessed through, our website is not incorporated by reference into this report. We have included our website address as a factual reference and do not intend it to be an active link to our website. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the Investor Relations section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the Securities and Exchange Commission, or the SEC. The public may read and copy any materials that we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site (http://www.sec.gov) that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC.

ITEM 1A. *RISK FACTORS*

Our business is subject to numerous risks. We cannot assure investors that our assumptions and expectations about our business will prove to have been correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. Such factors that could cause or contribute to such differences include those factors discussed below.

Our existing and potential stockholders should consider carefully the risks described below and the other information in this Annual Report, including under the heading Forward-Looking Statements and Risk Factors , our Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and the related notes. We may be unable, for many reasons, including those that are beyond our control, to implement our current business strategy. The following risks may result in material harm to our business, our financial condition and our results of operations. In that event, the market price of our common stock could decline.

Except as required by law, we do not undertake any obligation to update or revise any forward-looking statements contained in this Annual Report, whether as a result of new information, future events, or otherwise.

Risks Related to Our Business and Strategy

If we fail to obtain the additional capital necessary to fund our operations, we will be unable either to successfully develop and commercialize our product candidates or to finance the discovery and development of our next generation of product candidates.

Due to financial constraints, we recently discontinued development of Trizytek, our late-stage clinical candidate. We will require substantial future capital in order to complete the development and commercialization of our remaining clinical-stage product candidates, ALTU-238 and ALTU-237, and to conduct the research and development and clinical and regulatory activities necessary to bring our early stage research products and product candidates into clinical development. At this time, we have made a decision to allocate our financial, capital and human resources to

ALTU-238, are evaluating the feasibility of moving forward our

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early-stage clinical and pre-clinical programs and will make future decisions on these programs depending upon the availability of resources. Our future capital requirements will depend on many factors, including:

- the results of our Phase II pediatric clinical trial for ALTU-238 that we plan to begin in March 2009 and the results and costs of future clinical trials for ALTU-238 that we may initiate;
- any further non-clinical or clinical studies we may initiate based on the results of our Phase I clinical trial for ALTU-237 or discussions with regulatory authorities;
- the actual expenses of discontinuing the Trizytek program, including any contractual termination payments we are required to make;
- the timing, progress and results of ongoing manufacturing development work for ALTU-238;
- the results of our preclinical studies and testing for our early stage research products and product candidates, and any decisions to initiate clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates in clinical development, and any of our preclinical product candidates that progress to clinical trials;
- the cost of obtaining clinical and commercial supplies of active pharmaceutical ingredients, or APIs, and finished drug product in sufficient quantities for clinical development and any commercial launch;
- the costs of establishing commercial operations, including commercial manufacturing and distribution arrangements and sales, marketing and medical affairs functions, should any of our product candidates be approved and we participate in the launch;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our issued patents, seeking freedom to operate under any third party intellectual property rights, and defending intellectual property-related claims;
- our ability to establish and maintain collaborative or financing arrangements and obtain milestone, royalty and other payments from collaborators or third parties;
- the costs associated with our realignment plan, including termination of contractual obligations and facility-related costs; and
- the extent to which we acquire or invest in new businesses, products or technologies.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, or we decide it is necessary to preserve existing resources, we may find it necessary or appropriate to:

- stage, terminate or delay preclinical studies, clinical trials or other development activities for one or more of our product candidates; or
- delay our establishment of sales, marketing, medical affairs and commercial operations capabilities or other activities that may be necessary to commercialize our product candidates.

Our independent registered public accounting firm has included a going concern explanatory paragraph in its report for fiscal year ended December 31, 2008. This indicates that our recurring losses from operations and current lack of sufficient funds to sustain operations through the end of the following fiscal year raise substantial doubt about our ability to continue as a going concern. Our consolidated financial statements have been prepared on the basis of a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. If we became unable to continue as a going concern, we would have to liquidate our assets and might receive significantly less than the values at which they are carried on our consolidated financial statements. Any shortfall in the proceeds from the liquidation of our assets would directly reduce the amounts, if any, that holders of our common stock could receive in liquidation.

To remain a going concern, significant funding would be required. Our available funds will not be sufficient to fund the completion of the development and commercialization of any of our product candidates,

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including ALTU-238. We currently expect that our existing capital resources will be sufficient to maintain our current and planned operations into the fourth quarter of 2009. In addition, our operating plan may change as a result of many factors, including factors currently unknown to us, and we may need additional funds sooner than the end of 2009 and may seek such funds prior to that time. We are funding all costs related to the development ALTU-238 and cannot defer or avoid such expenses unless we delay or curtail the program, or we enter into a new collaboration agreement or secure alternative funding to support the development of ALTU-238. The failure to obtain additional financing or enter into a new collaboration could lead to a delay in or discontinuation of further development of ALTU-238. The inclusion of a going concern explanatory paragraph in the audit report of our registered public accounting firm for fiscal 2008 may materially and adversely affect our ability to raise new capital.

We are obligated under the terms of our redeemable preferred stock held by Vertex Pharmaceuticals Incorporated to make a significant payment upon the occurrence of a specified event. We may not have sufficient resources to make this payment when it becomes due.

If Vertex Pharmaceuticals Incorporated, or Vertex, the holder of our redeemable preferred stock, elects to redeem those shares on or after December 31, 2010, we will be required to pay an aggregate of $7.2 million plus dividends accrued after that date. We may require additional funding to make this payment. Funds for this purpose may not be available to us on favorable terms, or at all.

We may have contractual liabilities in connection with our discontinuation of the Trizytek program.

We have significant contractual obligations that we entered into with third parties for the Trizytek program. In connection with our discontinuation of this program and our new License Agreement with CFFTI, CFFTI may assume certain, but not all, of these obligations. In the case where CFFTI does not assume these obligations, we will need to negotiate a termination of these obligations with the third parties, which may involve the payment of termination fees or costs. For example, we have the right to terminate our agreement with Lonza in the event that we cease development or commercialization of Trizytek due to toxicity, efficacy or other technical or business considerations, in which case we must make a payment to Lonza if we have not already purchased from Lonza a specified value of APIs, which payment could be substantial.

We have a history of net losses, which we expect to continue for at least several years and, as a result, we are unable to predict the extent of any future losses or when, if ever, we will achieve, or be able to maintain, profitability.

We have incurred significant losses since 1999, when we were reorganized as a company independent from Vertex. At December 31, 2008, our accumulated deficit was $335.7 million, and we expect to continue to incur losses for at least the next several years. We have only been able to generate limited amounts of revenue from license and milestone payments under collaboration agreements, and payments for funded research and development, as well as revenue from products we no longer sell. Although our realignment of operations to focus on the development of ALTU-238 will result in a reduction in our annual research and development spending, we expect to continue to incur net operating losses for the next several years.

We must generate significant revenue to achieve and maintain profitability. All of our product candidates are still in development. Even if we succeed in developing and commercializing one or more of our product candidates, we may not be able to generate sufficient revenue to achieve or maintain profitability. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

Raising additional capital by issuing securities or through collaboration and licensing arrangements may cause dilution to existing stockholders, restrict our operations or require us to relinquish proprietary rights.

We may seek the additional capital necessary to fund our operations through public or private equity offerings, debt financings, or collaboration and licensing arrangements. To the extent that we raise additional

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capital through the sale of equity or convertible debt securities, existing stock ownership interests will be diluted, such dilution will in all likelihood be substantial, and the terms of such securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. In addition, many of the warrants that we have issued contain provisions that result in the reduction of the exercise price per share of such warrants to the extent we issue or are deemed to issue equity at a per share price less than the current exercise price of the warrants. At December 31, 2008, we had 3,095,606 such warrants outstanding, of which 1,962,494 warrants expired unexercised on February 1, 2009. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take actions such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish valuable development and commercialization rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us.

In order to fund our operations in the future, we may need to comply with NASDAQ Marketplace Rules that require stockholder approval of certain financings, which may limit our ability to raise sufficient capital.

The NASDAQ Marketplace Rules require us to obtain stockholder approval under certain circumstances if we issue outstanding equity securities that would comprise more than 20% of our total shares of common stock outstanding before the issuance of the securities. In order to fund our operations in the future, we may need to obtain stockholder approval in order to comply with these rules, and we may not be successful in obtaining any such stockholder approval. If we failed to obtain such an approval prior to a financing, our funding options would be limited, which would adversely affect our ability to successfully develop and commercialize our product candidates or to finance the discovery and development of our next generation of product candidates.

Our competitors may develop products that are less expensive, safer or more effective, which may diminish or prevent the commercial success of any product candidate that we bring to market.

Competition in the pharmaceutical and biotechnology industries is intense. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies engaged in drug discovery activities, both in the United States and abroad. Some of these competitors have greater financial resources than we do, greater experience in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing than we do, and have products or are pursuing the development of product candidates that target the same diseases and conditions that are the focus of our drug development programs, including those set forth below.

ALTU-238. If approved, ALTU-238, the product candidate we are developing as a once-weekly treatment for human growth hormone, or hGH, deficiency and related disorders, will compete with existing approved hGH therapies from companies such as BioPartners, Eli Lilly, Genentech, Merck Serono, Novo Nordisk, Pfizer, Sandoz, and Teva Pharmaceutical Industries. In addition, we understand that ALTU-238 may compete with product candidates in clinical development from some of these companies and others, including LG Life Sciences, which is developing a long-acting hGH therapy based on an encapsulated microparticle technology, and Ambrx Inc., which is also developing a long-acting hGH therapy in conjunction with Serono.

*ALTU-*237. If approved, ALTU-237, the product candidate we may further develop for the treatment of hyperoxalurias, depending on the availability of funding, may compete with product candidates in development at companies such as Amsterdam Molecular Therapeutics, Medix, NephroGenex, and OxThera.

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We may not be successful in establishing and maintaining collaborations on acceptable terms, which could adversely affect our ability to develop and commercialize our products.

An element of our business strategy is to establish collaborative arrangements with third parties with regard to development, regulatory approval, sales, marketing and distribution of our products. We may collaborate with other companies to accelerate the development of some of our early-stage product candidates, to develop and commercialize or co-commercialize our more mature product candidates or to advance other business objectives. The process of establishing new collaborative relationships is difficult, time-consuming and involves significant uncertainty. We face, and will continue to face, significant competition in seeking appropriate collaborators. Moreover, if we do establish collaborative relationships, our collaborators may fail to fulfill their responsibilities or seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, a change in business strategy, a change of control or other reasons. In the event of a termination, we may incur termination payments or other expenses in connection with any reacquisition of rights. For example, in connection with the termination of our collaboration with Genentech for ALTU-238, we became solely responsible for all expenses in connection with the ALTU-238 program. If we are unable to establish and maintain collaborative relationships on acceptable terms, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of funding.

If we enter into new collaborative agreements, our collaborators and we may not achieve our projected research and development goals in the time frames we announce and expect, which could have an adverse impact on our business and could cause our stock price to decline.

If we enter into new collaborative agreements for our product candidates, we expect to set goals for and make public statements regarding the timing of activities, such as the commencement and completion of preclinical studies and clinical trials, anticipated regulatory approval dates and developments and milestones under those collaboration agreements. The actual timing of such events can vary dramatically due to a number of factors such as delays or failures in our or our collaborators preclinical studies or clinical trials, delays or failures in manufacturing process development activities or in manufacturing product candidates, the amount of time, effort and resources to be committed to our programs by our future collaborators, delays in filing for regulatory approval, and the uncertainties inherent in the regulatory approval process, including delays in obtaining regulatory approval. We cannot be certain that our or our collaborators preclinical studies and clinical trials will advance or be completed in the time frames we announce or expect, that our collaborators or we will make regulatory submissions or receive regulatory approvals as planned or that our collaborators or we will be able to adhere to our current schedule for the achievement of key milestones under any of our internal or collaborative programs. If our collaborators or we fail to achieve one or more of these milestones as planned, our business will be materially adversely affected and the price of our common stock could decline.

Risks Related to Development of Our Product Candidates

If we, or if we enter into future collaborative agreements, our collaborators, are unable to commercialize our lead product candidates, or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our time and financial resources to date in the development of oral and injectable crystallized protein therapies, including Trizytek (for which we have discontinued development), ALTU-238 and ALTU-237 (the development of which is on hold until sufficient additional funding can be secured), for the treatment of gastrointestinal and metabolic disorders. Our ability and the ability of a collaborative partner to develop and commercialize our current product candidates successfully, and therefore our ability to generate revenues, will depend on numerous factors, including:

successfully scaling up the manufacturing processes for our product candidates, successfully completing stability testing and release of our product candidates, and obtaining sufficient supplies of, our product candidates, in order to complete our clinical trials and toxicology studies on a timely basis;

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receiving marketing approvals from the FDA and foreign regulatory authorities;

arranging for commercial-scale supplies of our product candidates with contract manufacturers whose manufacturing facilities operate in compliance with current good manufacturing practice regulations, or cGMPs, including the need to scale up the manufacturing process for commercial scale supplies;

establishing sales, marketing and distribution capabilities on our own, through collaborative agreements or through third parties;

obtaining commercial acceptance of our product candidates, if approved, in the medical community and by third-party payors and government pricing authorities; and

establishing favorable pricing from foreign regulatory authorities.

If we are not successful in commercializing ALTU-238 or are significantly delayed in doing so, our business will be materially harmed.

Because our product candidates are in clinical development, there is a significant risk of failure.

Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA, and even fewer are approved for commercialization. We will only receive regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA or the applicable foreign regulatory authority, in well-designed and controlled clinical trials, that the product candidate is safe and effective and otherwise meets the appropriate standards required for approval for a particular indication. Clinical trials are lengthy, complex and extremely expensive programs with uncertain results. A failure of one or more of our clinical trials may occur at any stage of testing. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA.

A number of events or factors, including any of the following, could delay the completion of our ongoing and planned clinical trials and negatively impact our ability to submit an NDA and obtain regulatory approval for, and to market and sell, a particular product candidate, including our clinical-stage product candidates:

conditions imposed by us or imposed on us by the FDA or any foreign regulatory authority regarding the scope or design of our clinical trials;

delays in obtaining, or our inability to obtain or maintain, required approvals from institutional review boards, or IRBs, or other reviewing entities at clinical sites selected for participation in our clinical trials;

negative or inconclusive results from clinical trials, or results that are inconsistent with earlier results, that necessitate additional clinical studies;

delays in the completion of manufacturing development work for our product candidates, and in collecting the necessary manufacturing information for submission of our marketing approval applications for our product candidates;

any dispute that arises under our current or future collaborative agreements or our agreements with third parties;

insufficient supply or deficient quality of our product candidates or other materials necessary to conduct our clinical trials;

difficulties enrolling subjects in our clinical trials, including, for example, finding pediatric subjects with hGH deficiency who have not previously received hGH therapy for our pediatric trials of ALTU-238;

serious or unexpected side effects experienced by subjects in clinical trials; or

failure of our third-party contractors or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations to us in a timely manner.

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Delays in or inconclusive results from our clinical trials may result in increased development costs for our product candidates and corresponding delays in the filing of an NDA for product candidates and the receipt of marketing approval for the product candidate or discontinuation of a program, which could cause our stock price to decline and could limit our ability to obtain additional financing. For example, our stock price declined significantly following the announcement of the results of our Phase III clinical trial for Trizytek. In addition, we were unable to secure a corporate partnership for Trizytek following the announcement of such results and consequently decided to discontinue the Trizytek program. In addition, if one or more of our product candidates are delayed, our competitors may be able to bring products to market before we do, and the commercial advantage, profitability or viability of our product candidates, including our clinical-stage product candidates, could be significantly reduced.

We have not yet completed a full Phase III program for any of our product candidates in clinical development, other than for the Trizytek program, which was discontinued in January 2009, and we have not advanced, and may never advance, our product candidates that are currently in preclinical testing into clinical trials. Even if our trials are successful, we may still be required or may determine it is desirable to perform additional studies for approval or in order to achieve a broad indication for the labeling of the drug.

For the ALTU-238 program, we have completed Phase I clinical trials in healthy adults and a Phase II clinical trial in adults with hGH deficiency and have commenced a Phase II clinical trial in children with hGH deficiency. The efficacy of ALTU-238 has not yet been tested in a human clinical trial, and ALTU-238 may prove not to be clinically effective as an extended-release formulation of hGH. In addition, it is possible that patients receiving ALTU-238 will suffer additional or more severe side effects than we observed in our earlier Phase I and Phase II clinical trials, which could delay or preclude regulatory approval of ALTU-238 or limit its commercial use.

If we observe serious or other adverse events during the time our product candidates are in development or after our products are approved and on the market, we may be required to perform lengthy additional clinical trials, may be denied regulatory approval of such products, may be forced to change the labeling of such products or may be required to withdraw any such products from the market, any of which would hinder or preclude our ability to generate revenues.

As our clinical trials progress or increase in size or the medical conditions of the population in which we are testing our products vary, the potential for serious or other adverse events related or unrelated to our product candidates could vary and possibly increase. If the incidence of these events increases in number or severity, if a regulatory authority believes that these events constitute an adverse effect caused by the drug, or if other effects are identified either during future clinical trials or after any of our drug candidates are approved and on the market:

- we may be required to conduct additional preclinical or clinical trials, make changes in clinical trial brochures or, if a product is approved, make changes to the labeling of any such products, reformulate any such products, or implement changes to or obtain new approvals of our or our contractors or collaborators manufacturing facilities or processes;
- regulatory authorities may be unwilling to approve our product candidates or may withdraw approval of our products;
- we may experience a significant drop in the sales of the affected products;
- our reputation in the marketplace may suffer; and
- we may become the target of lawsuits, including class action suits.

Any of these events could prevent approval or harm sales of the affected products or could substantially increase the costs and expenses of commercializing and marketing any such products.

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We may fail to select or capitalize on the most scientifically, clinically or commercially promising or profitable indications or therapeutic areas for our product candidates.

We have limited technical, managerial and financial resources to determine the indications on which we should focus the development efforts related to our product candidates. We may make incorrect determinations. Our decisions to allocate our research, management and financial resources toward particular indications or therapeutic areas for our product candidates may not lead to the development of viable commercial products and may divert resources from better opportunities. Similarly, our decisions to delay or terminate drug development programs may also be incorrect and could cause us to miss valuable opportunities. For example, we have made a decision to allocate substantially all of our existing financial, capital and human resources to ALTU-238, and are evaluating the feasibility of moving forward our early-stage clinical and pre-clinical programs and will make future decisions on these programs depending upon the availability of resources. If we invest in the advancement of a candidate that proves not to be viable, we will have fewer resources available for potentially more promising candidates.

Risks Related to Regulatory Approval of Our Product Candidates and Other Government Regulations

If we or our future collaborators do not obtain required regulatory approvals, we will be unable to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

ALTU-238, ALTU-237 and any other product candidates we may discover or acquire and seek to commercialize, either alone or in conjunction with a collaborator, are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries relating to the testing, manufacture, safety, efficacy, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, sale and distribution of drugs. In the United States and in many foreign jurisdictions, we must successfully complete rigorous preclinical testing and clinical trials and an extensive regulatory review process before a new drug can be sold. We have not obtained regulatory approval for any product. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays.

The time required to obtain approval by the FDA is unpredictable but typically takes many years following the commencement of clinical trials, depending upon numerous factors, including the complexity of the product candidate and the disease to be treated. Our product candidates may fail to receive regulatory approval for many reasons, including:

a failure to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for a particular indication;

the results of clinical trials may not meet the level of statistical significance required by the FDA or other regulatory authorities for approval;

an inability to demonstrate that a product candidate s benefits outweigh its risks;

an inability to demonstrate that the product candidate presents an advantage over existing therapies;

the FDA s or comparable foreign regulatory authorities disagreement with the manner in which our collaborators or we interpret the data from preclinical studies or clinical trials;

the FDA s or comparable foreign regulatory authorities failure to approve the manufacturing processes or facilities of third-party contract manufacturers of clinical and commercial supplies; and

a change in the approval policies or regulations of, or the specific advice provided to us by, the FDA or comparable foreign regulatory authorities or a change in the laws governing the approval process.

The FDA or comparable foreign regulatory authorities might decide that the data are insufficient for approval and require additional clinical trials or other studies. Furthermore, even if we do receive regulatory approval to market a commercial product, any such approval may be subject to limitations on the indicated uses for which our collaborative partner or we may market the product or may be subject to post-approval commitments to conduct Phase IV studies, patient monitoring or other risk management measures that could

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require significant financial resources. It is possible that none of our existing or future product candidates will ever obtain the appropriate regulatory approvals necessary for us or our collaborators to begin selling them.

Failure to obtain regulatory approvals or to comply with regulatory requirements in foreign jurisdictions would prevent us or any collaborator from marketing our products internationally.

We intend to have our product candidates marketed outside the United States. In order to market products in the European Union and many other non-United States jurisdictions, our collaborators or we must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. We have no experience in obtaining foreign regulatory approvals for our product candidates. The approval procedures vary among countries and can involve additional and costly preclinical and clinical testing and data review. The time required to obtain approval in other countries may differ from that required to obtain FDA approval. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. We also face challenges arising from the different regulatory requirements imposed by United States and foreign regulators with respect to clinical trials. The EMEA often imposes different requirements than the FDA with respect to the design of a pivotal Phase III clinical trial. Our future collaborators or we may not receive necessary approvals to commercialize our products in any market. The failure to obtain these approvals could harm our business and result in decreased revenues from the sale of products or from milestones or royalties associated with any collaboration agreements we may enter into in the future.

Our product candidates will remain subject to ongoing regulatory requirements even if they receive marketing approval, and if we fail to comply with these requirements, we could lose these approvals, and the sales of any approved commercial products could be suspended.

Even if we receive regulatory approval to market a particular product candidate, the product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and record keeping. In addition, the approval may be subject to limitations on the uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, which could reduce our revenues, increase our expenses and render the approved product candidate not commercially viable.

In addition, as clinical experience with a drug increases after approval because it is typically used by a larger and more diverse group of patients after approval than during clinical trials, side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials or other studies. Any adverse effects observed after the approval and marketing of a product candidate could result in limitations on the use of or withdrawal of any approved products from the marketplace. Absence of long-term safety data may also limit the approved uses of our products, if any. If we fail to comply with the regulatory requirements of the FDA and other applicable United States and foreign regulatory authorities, or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including:

- restrictions on the products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;

injunctions;

product seizures or detentions;

import or export bans or restrictions;

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voluntary or mandatory product recalls and related publicity requirements;

suspension or withdrawal of regulatory approvals;

total or partial suspension of production; and

refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

If we are slow to adapt, or are unable to adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, we may lose marketing approval for our products when and if any of them are approved, resulting in decreased revenue from milestones, product sales or royalties. Moreover, even when a manufacturer has fully complied with applicable regulatory standards, products manufactured and distributed may ultimately fail to comply with applicable specifications, leading to product withdrawals or recalls.

We deal with hazardous materials and must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our activities and those of our third-party manufacturers on our behalf involve the controlled storage, use and disposal of hazardous materials, including microbial agents, corrosive, explosive and flammable chemicals and other hazardous compounds. Our manufacturers and we are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials.

In the event of an accident, state or federal authorities may curtail our use of these materials and interrupt our business operations. In addition, we could be liable for any resulting civil damages which may exceed our financial resources and may seriously harm our business. While we believe that the amount of insurance we currently carry, providing coverage of $1.0 million, should be sufficient for typical risks regarding our handling of these materials, it may not be sufficient to cover pollution conditions or other extraordinary or unanticipated events. Furthermore, an accident could damage, or force us to shut down, our operations. In addition, if we develop manufacturing capability, we may incur substantial costs to comply with environmental regulations and would be subject to the risk of accidental contamination or injury from the use of hazardous materials in our manufacturing process.

Risks Related to Our Dependence on Third Parties

We have no manufacturing capacity, and we have relied and expect to continue to rely on third-party manufacturers to produce our product candidates.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates or any of the compounds that we are testing in our preclinical programs, and we lack the internal resources and the capabilities to do so. As a result, we currently rely, and we expect to rely in the future, on third-party manufacturers to supply the APIs for our product candidates and to produce and package final drug products, if and when they are approved for marketing. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates or products ourselves, including:

reliance on the third party for manufacturing process development, sourcing of key raw materials and specialized manufacturing equipment, regulatory compliance and quality assurance;

limitations on supply availability resulting from capacity and scheduling constraints of the third party;

the possible breach of the manufacturing agreement by the third party because of factors beyond our control; and

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the possible termination or non-renewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop our product candidates and commercialize any products that receive regulatory approval on a timely basis.

We currently rely on a limited number of manufacturers for the clinical and commercial supply of each of our product candidates, which could delay or prevent the clinical development and commercialization of our product candidates.

We currently depend on single source suppliers for ALTU-238. Any disruption in production, inability of a supplier to produce adequate quantities of clinical and other material to meet our needs or other impediments could adversely affect our ability to successfully complete the clinical trials and other studies of our product candidates, delay submissions of our regulatory applications or adversely affect our ability to commercialize our product candidates in a timely manner, or at all.

We have purchased the hGH, the API in ALTU-238, for our prior and ongoing clinical trials from Sandoz GmbH, or Sandoz. We have also produced ALTU-238 for these trials and believe that the current scale of manufacturing is sufficient to support the planned Phase III program for ALTU-238 in both adult and pediatric growth hormone deficient patients. In July 2008, Sandoz and we entered into a long term supply agreement, which has an initial term expiring in 2012, with an optional two year extension period. Because we do not have another long term supplier of hGH in place, any disruption in Sandoz ability to supply us with hGH as needed would adversely affect the ALTU-238 program.

We have an agreement with Althea for Althea to use the hGH supplied to it to produce the clinical supplies for our planned clinical trials of ALTU-238. Any delay in the production, testing and release of ALTU-238 could delay our planned clinical trials and result in additional unforeseen expenses.

Our agreement with Althea covers only the manufacture of ALTU-238 for the planned clinical trials of ALTU-238. We will need to negotiate an additional agreement under which Althea would provide the commercial supply of ALTU-238 or find an alternative commercial manufacturer. Switching manufacturers would require cooperation with Althea, technology transfers, training, and validation of the alternative manufacturer s processes, and, under some circumstances, will require us to make a specified payment to Althea. Changes in manufacturing processes or procedures, including a change in the location where the drug is manufactured or a change of a third-party manufacturer, may require prior review and approval from the FDA and satisfaction of comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch of a product. If we are unable to secure another contract manufacturer for ALTU-238 at an acceptable cost, the commercialization of ALTU-238 could be delayed, prevented or impaired, and the costs related to ALTU-238 may increase. Any dispute over the terms of, or decisions regarding, our collaboration with Althea or other adverse developments in our relationship would materially harm our business and might accelerate our need for additional capital.

Our contract manufacturers may encounter difficulties or unforeseen expenses in connection with the commercial scale-up of manufacturing activities for our product candidates

We do not have any agreements in place to manufacture our product candidates, other than the API for ALTU-238, on a commercial scale. In order to commercialize ALTU-238, we, in conjunction with Althea, will need to scale up the manufacturing of ALTU-238 drug product. We may be required to fund capital improvements to support scale-up of

manufacturing and related activities. Althea may not be able to increase its manufacturing capacity and we may need to find an alternative supplier. In addition, Sandoz may discontinue its manufacturing of hGH, in which case we would need to find an alternative source. It may be difficult for us to enter into additional supply arrangements on a timely basis or on acceptable terms, which could delay or prevent our ability to commercialize ALTU-238.

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Any performance failure on the part of a contract manufacturer could delay clinical development or regulatory approval of our product candidates or commercialization of any approved products.

The failure of a contract manufacturer to achieve and maintain high manufacturing standards could result in patient injury or death, product liability claims, product recalls, product seizures or withdrawals, delays or failures in testing or delivery, cost overruns, failure of regulatory authorities to grant marketing approvals, delays, suspensions or withdrawals of approvals, injunctions, fines, civil or criminal penalties, or other problems that could seriously harm our business. Contract manufacturers may encounter difficulties involving production yields, quality control and quality assurance. These manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state and foreign agencies which audit strict compliance with cGMP and other applicable government regulations and corresponding foreign standards. However, we or a future collaborator may have limited control over third-party manufacturers compliance with these regulations and standards. Present or future manufacturers might not be able to comply with cGMP and other FDA or international regulatory requirements.

We rely on third parties to conduct, supervise and monitor our clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such trials.

We rely on third parties such as contract research organizations, medical institutions and clinical investigators to enroll qualified patients and conduct, supervise and monitor our clinical trials. Our reliance on these third parties for clinical development activities reduces our control over these activities. Our reliance on these third parties, however, does not relieve us of our regulatory responsibilities, including ensuring that our clinical trials are conducted in accordance with good clinical practice regulations and the investigational plan and protocols contained in the IND. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. In addition, they may not complete activities on schedule, or may not conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our trial design. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, our efforts to obtain regulatory approvals for, and commercialize, our product candidates may be delayed or prevented.

Because we may enter into in the future sales or collaboration transactions, we may be dependent upon our collaborators, and we may be unable to prevent them from taking actions that may be harmful to our business or inconsistent with our business strategy.

Any future licensing and collaboration agreements that we may enter into with respect to our product development candidates may reduce or eliminate the control we have over the development and commercialization of our product candidates. Our future collaborators may decide to terminate a development program under circumstances where we might have continued such a program, or may be unable or unwilling to pursue ongoing development and commercialization activities as quickly as we would prefer. A collaborator may follow a different strategy for product development and commercialization that could delay or alter development and commercial timelines and likelihood of success. A collaborator may also be unwilling or unable to fulfill its obligations to us, including its development and commercialization responsibilities. Any future collaborators will likely have significant discretion in determining the efforts and level of resources that they dedicate to the development and commercialization of our product candidates. In addition, although we seek to structure our agreements with potential collaborators to prevent the collaborator from developing and commercializing a competitive product, we are not always able to negotiate such terms and the possibility exists that our collaborators may develop and commercialize, either alone, or with others or through an in-license or acquisition, products that are similar to or competitive with the products that are the subject of the collaboration with us. If any collaborator terminates its collaboration with us or fails to perform or satisfy its obligations to us, the development, regulatory approval or commercialization of our product candidate would be delayed or may not occur and our business and prospects could be materially and adversely affected. Likewise, if we fail to fulfill our obligations under a collaboration and license agreement, our collaborator

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may be entitled to damages, to terminate the agreement, or terminate or reduce its financial payment obligations to us under our collaborative agreement.

Our collaborations with outside scientists and consultants may be subject to restriction and change.

We work with chemists, biologists and other scientists at academic and other institutions, and consultants who assist us in our research, development, regulatory and commercial efforts. These scientists and consultants have provided, and we expect that they will continue to provide, valuable advice on our programs. These scientists and consultants are not our employees, may have other commitments that would limit their future availability to us and typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, we will be unable to prevent them from establishing competing businesses or developing competing products. For example, if a key principal investigator identifies a potential product or compound that is more scientifically interesting to his or her professional interests, his or her availability could be restricted or eliminated.

Risks Related to Commercialization of Our Product Candidates

If physicians and patients do not accept our future products, we may be unable to generate significant revenue, if any.

Even if we or a future collaborator receives regulatory approval for our product candidates, these product candidates may not gain market acceptance among physicians, healthcare payors, government pricing agencies, patients or the medical community. Physicians may elect not to recommend or patients may elect not to use these products for a variety of reasons, including:

- prevalence and severity of adverse side effects;
- ineffective marketing and distribution support;
- timing of market introduction of competitive products;
- lack of availability of, or inadequate reimbursement from managed care plans and other third-party or government payors;
- lower demonstrated clinical safety and efficacy compared to other products;
- other potential advantages of alternative treatment methods; and
- lack of cost-effectiveness or less competitive pricing.

If our approved drugs fail to achieve market acceptance, we will not be able to generate significant revenue, if any.

If the government and third-party payors fail to provide coverage and adequate payment rates for our future products, if any, our revenue and prospects for profitability will be harmed.

In both domestic and foreign markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. These third-party payors are increasingly attempting to contain healthcare costs by demanding price discounts or rebates and limiting

both coverage on which drugs they will pay for and the amounts that they will pay for new drugs. As a result, they may not cover or provide adequate payment for our drugs.

In the United States there have been, and we expect that there will continue to be, a number of federal and state proposals to implement governmental pricing reimbursement controls. The Medicare Prescription Drug and Modernization Act of 2003 imposed new requirements for the distribution and pricing of prescription drugs that may affect the marketing of our products, if we obtain FDA approval for those products. Under this law, Medicare was extended to cover a wide range of prescription drugs other than those directly administered by physicians in a hospital or medical office. Competitive regional private drug plans were authorized to

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establish lists of approved drugs, or formularies, and to negotiate rebates and other price control arrangements with drug companies. Proposals to allow the government to negotiate Medicare drug prices with drug companies directly, if enacted, might further constrain drug prices, leading to reduced revenues and profitability. While we cannot predict whether any future legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability.

Foreign governments tend to impose strict price controls on pharmaceutical products, which may adversely affect our revenues, if any.

In some foreign countries, particularly the countries of the European Union, Canada and Japan, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In some countries, the pricing is limited by the pricing of existing or comparable therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to enter into collaborative development and commercialization agreements and our revenues from these agreements could be adversely affected.

There is a substantial risk of product liability claims in our business. If we are unable to obtain sufficient insurance, a product liability claim against us could adversely affect our business.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face even greater risks upon any commercialization by us of our product candidates. We have product liability insurance covering our clinical trials in the amount of $10 million, which we believe is adequate to cover any current product liability exposure we may have. However, liabilities may exceed the extent of our coverage, resulting in material losses. Clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance or increase our existing coverage at a reasonable cost to protect us against losses that could have a material adverse effect on our business. An individual may bring a product liability claim against us if one of our products or product candidates causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

liabilities that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available;

an increase of our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, or at all;

withdrawal of clinical trial volunteers or patients;

damage to our reputation and the reputation of our products, resulting in lower sales;

regulatory investigations that could require costly recalls or product modifications;

litigation costs; and

the diversion of management s attention from managing our business.

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Risks Related to Our Intellectual Property

If the combination of patents, trade secrets and contractual provisions that we rely on to protect our intellectual property is inadequate to provide us with market exclusivity, our ability to successfully commercialize our product candidates will be harmed and we may not be able to operate our business profitably.

Our success depends, in part, on our ability to obtain, maintain and enforce our intellectual property rights both domestically and abroad. The patent position of biotechnology companies is generally highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The validity, enforceability and commercial value of our rights, therefore, are highly uncertain.

Our patents may not protect us against our competitors. The issuance of a patent is not conclusive as to its scope, validity or enforceability. The scope, validity or enforceability of our patents can be challenged in litigation. Such litigation is often complex, can involve substantial costs and distraction and the outcome of patent litigation is often uncertain. If the outcome is adverse to us, third parties may be able to use our patented inventions and compete directly with us, without payment to us. Third parties may also be able to circumvent our patents by design innovations. We may not receive any additional patents based on the applications that we have filed and are currently pending.

Because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing or, in some cases, not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, neither we nor our licensors or collaborators can be certain that they or we were the first to make the inventions claimed in patents or pending patent applications, or that they or we were the first to file for protection of the inventions set forth in these patent applications. Assuming the other requirements for patentability are met, in the United States, the first to make the claimed invention is entitled to the patent, and outside the United States, the first to file is entitled to the patent.

Many of the proteins that are the APIs in our product candidates are off-patent. Therefore, we have obtained and are seeking to obtain patents directed to novel compositions of matter, formulations, methods of manufacturing and methods of treatment to protect some of our products. Such patents may not, however, prevent our competitors from developing products using the same APIs but different manufacturing methods or formulation technologies that are not covered by our patents.

If third parties successfully assert that we have infringed their patents and proprietary rights or challenge the validity of our patents and proprietary rights, we may become involved in intellectual property disputes and litigation that would be costly, time consuming, and could delay or prevent the development or commercialization of our product candidates.

Our ability to commercialize our product candidates depends on our ability to develop, manufacture, market and sell our product candidates without infringing the proprietary rights of third parties. Third parties may allege our product candidates infringe their intellectual property rights. Numerous United States and foreign patents and pending patent applications that are owned by third parties exist in fields that relate to our product candidates and our underlying technology, including patents and patent applications claiming compositions of matter of, methods of manufacturing, and methods of treatment using, specific proteins, combinations of proteins, and protein crystals. For example, we are aware of some issued United States and/or foreign patents that may be relevant to the development and commercialization of our product candidates. However, we believe that, if these patents were asserted against us, it is likely that we would not be found to infringe any valid claim of the patents relevant to our development and commercialization of these products. If any of these patents were asserted against us and determined to be valid and

construed to cover any of our product candidates, including, without limitation, ALTU-238 and ALTU-237, our development and commercialization of these products could be materially adversely affected.

Although we believe it is unlikely that we would be found to infringe any valid claim of these patents, we may not succeed in any action in which the patents are asserted against us. In order to successfully challenge the validity of any United States patent, we would need to overcome a presumption of validity. This

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burden is a high one requiring clear and convincing evidence. If any of these patents were found to be valid and we were found to infringe any of them, or any other patent rights of third parties, we would be required to pay damages, stop the infringing activity or obtain licenses in order to use, manufacture or sell our product candidates. Any required license might not be available to us on acceptable terms, or at all. If we succeeded in obtaining these licenses, payments under these licenses would reduce any earnings from our products. In addition, some licenses might be non-exclusive and, accordingly, our competitors might gain access to the same technology as that which was licensed to us. If we failed to obtain a required license or were unable to alter the design of our product candidates to make the licenses unnecessary, we might be unable to commercialize one or more of our product candidates, which could significantly affect our ability to establish and grow our commercial business.

In order to protect or enforce our patent rights, defend our activities against claims of infringement of third-party patents, or to satisfy contractual obligations to licensees of our own intellectual property, we might be required to initiate patent litigation against third parties, such as infringement suits or nullity, opposition or interference proceedings. Our collaborators or we may enforce our patent rights under the terms of our major collaboration and license agreements, but neither we nor our collaborators is required to do so. In addition, others may sue us for infringing their patent rights or file nullity, opposition or interference proceedings against our patents, even if such claims are without merit.

Intellectual property litigation is relatively common in our industry and can be costly. Even if we prevail, the cost of such litigation could deplete our financial resources. Litigation is also time consuming and could divert management s attention and resources away from our business. Furthermore, during the course of litigation, confidential information may be disclosed in the form of documents or testimony in connection with discovery requests, depositions or trial testimony. Disclosure of our confidential information and our involvement in intellectual property litigation could materially adversely affect our business. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could significantly limit our ability to continue our operations.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. While we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have inadvertently or otherwise used or disclosed intellectual property, trade secrets or other proprietary information of any such employee s former employer. Litigation may be necessary to defend against these claims and, even if we are successful in defending ourselves, could result in substantial costs or be distracting to management. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel.

If we are unable to protect our trade secrets, we may be unable to protect our interests in proprietary technology, processes and know-how that is not patentable or for which we have elected not to seek patent protection.

In addition to patented technology, we rely upon unpatented proprietary technology, processes and know-how, including particularly our manufacturing know-how relating to the production of the crystallized proteins used in the formulation of our product candidates. In an effort to protect our unpatented proprietary technology, processes and know-how, we require our employees, consultants, collaborators, contract manufacturers and advisors to execute confidentiality agreements. These agreements, however, may not provide us with adequate protection against improper use or disclosure of confidential information, in particular as we are required to make such information available to a larger pool of people as we seek to increase production of our product candidates and their component proteins. These agreements may be breached, and we may not become aware of, or have adequate remedies in the event of, any such breach. In addition, in some situations, these agreements may conflict with, or be subject to, the

rights of third parties with whom our employees, consultants, collaborators, contract manufacturers or advisors have previous employment or consulting relationships. Also, others may independently develop substantially equivalent technology, processes and know-how or otherwise gain access to our trade secrets. If we are unable to protect the confidentiality of our

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proprietary technology, processes and know-how, competitors may be able to use this information to develop products that compete with our products, which could adversely impact our business.

If we fail to comply with our obligations in the agreements under which we licensed development, commercialization or other technology rights to products or technology from third parties, we could lose license rights that are important to our business or incur financial obligations based on our exercise of such license rights.

Some of our license agreements provide for licenses to us of technology that is important to our business, and we may enter into additional agreements in the future that provide licenses to us of valuable technology. These licenses impose, and future licenses may impose, various commercialization, milestone and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license even where we are able to achieve a milestone or cure a default after a date specified in an agreement, in which event we would lose valuable rights and our ability to develop our product candidates.

Risks Related to Our Employees and Growth

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

We are a small company with 145 employees as of December 31, 2008. In 2009, we underwent a strategic realignment, which resulted in an approximate 75% headcount reduction. Our success depends on our ability to attract, retain and motivate highly qualified management, development and scientific personnel, which may be made more difficult as a result of the realignment. In particular, we are highly dependant on our new President and Chief Executive Officer, Dr. Georges Gemayel, and the other principal members of our executive, development and scientific teams.

All of the arrangements we have with the key members of our executive, development and scientific teams may be terminated by us or the employee at any time without notice. Although we do not have any reason to believe that we may lose the services of any of these persons in the foreseeable future, the loss of the services of any of these persons might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified development and scientific personnel and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of development and scientific personnel from universities and research institutions. We do not maintain key person insurance on any of our employees.

As we evolve from a company primarily involved in drug research and development into one that may become involved in the commercialization of drug products, we may have difficulty managing our growth, which could disrupt our operations.

As we advance our drug candidates through the development process, we will need to expand our development, regulatory, manufacturing, sales and marketing capabilities or contract with other organizations to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various contract manufacturers, collaborative partners, suppliers and other organizations. Our ability to manage our operations and growth requires us to continue to improve our operational, financial and management controls, reporting systems and procedures. Such growth could place a strain on our management, administrative and operational infrastructure. We may not be able to make improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. In addition,

the physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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Risks Related to Our Common Stock and Public Company Compliance Requirements

Our stock price has been and is likely to continue to be volatile.

Investors should consider an investment in our common stock as risky and subject to significant loss and wide fluctuations in market value. Our common stock has only been publicly traded since January 26, 2006, and accordingly there is a limited history on which to gauge the volatility of our stock price. Our stock price has, however, been volatile since we began to be publicly traded. For example, our stock price declined approximately 50% following our announcement that our collaboration with Genentech had been terminated in December 2007. Our stock price also declined sharply following our announcement of the top line data of our Phase III efficacy trial of Trizytek in August 2008 and in connection with the announcement of our strategic realignment in January 2009. The stock market as a whole has experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks may not relate to the operating performance of the companies represented by the stock. In addition, we may not continue to qualify for continued listing on The NASDAQ Global Market. To maintain listing, we are required, among other things, to maintain a daily closing bid price of $1.00 and a minimum market value of publicly held shares of $5.0 million. NASDAQ has suspended enforcement of its rules requiring a minimum $1.00 closing bid price and a minimum market value of publicly held shares of $5.0 million through April 20, 2009.

The market price of our common stock has been between $0.16 and $19.79 per share from January 1, 2007 until March 6, 2009. Some of the factors that may cause the market price of our common stock to continue to fluctuate include:

- delays in or results from our clinical trials or studies;
- our entry into or the loss of a significant collaboration or the expansion or contraction of a significant collaboration, disputes with a collaborator, or delays in the progress of a collaborative development program;
- competitive product information such as results of clinical trials conducted by others on drugs that would compete with our product candidates or the regulatory filing or approval of such competitive products;
- delays or other problems with manufacturing our product candidates or approved products;
- failure or delays in advancing product candidates from our preclinical programs, or other product candidates we may discover or acquire in the future, into clinical trials;
- failure or discontinuation of any of our research programs;
- regulatory review delays, changes in regulatory requirements, new regulatory developments or enforcement policies in the United States and foreign countries;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by us or our competitors;
- changes in estimates or recommendations by securities analysts, if any, who cover our common stock;
- failure to meet estimates or recommendations by securities analysts, if any, who cover our common stock;

positive or negative publicity regarding our product candidates or any approved products;

litigation or threatened litigation;

sales, future sales or anticipated sales of our common stock by us or our stockholders;

changes in the structure of health care payment systems;

failure of any of our product candidates, if approved, to achieve commercial success;

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economic and other external factors or other disasters or crises;

period-to-period fluctuations in our financial results; and

general market conditions.

These and other external factors may cause the market price and demand for our common stock to fluctuate substantially, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In addition, in the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit regardless of the validity of the claims or the ultimate outcome. Such a lawsuit could also divert the time and attention of our management and create additional volatility in our common stock price.

One of our stockholders has substantial influence over us which could delay or prevent a change in corporate control or result in the entrenchment of management and the board of directors.

Entities affiliated with Warburg Pincus Private Equity VIII, L.P., or Warburg Pincus, one of our principal stockholders, are entitled to designate up to two individuals as candidates to our board of directors, for so long as Warburg Pincus owns at least 2,691,935 shares of our common stock, or one individual for so long as Warburg Pincus owns at least 1,794,623 shares of our common stock. We have agreed to nominate and use our reasonable efforts to cause the election of such candidates. Stewart Hen and Jonathan S. Leff were the members of our board of directors designated by Warburg Pincus, but each of these individuals resigned as Directors effective December 31, 2008, and Warburg Pincus has not designated any candidates to replace them.

A significant portion of our total outstanding shares may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. We had 31,131,056 shares of common stock outstanding as of March 6, 2009. Holders of up to approximately 7.8 million shares of our common stock, assuming the exercise of warrants to purchase shares of our common stock, have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have registered all shares of common stock issuable under our equity compensation plans and they can now be freely sold in the public market upon issuance. A decline in the price of shares of our common stock might impede our ability to raise capital through the issuance of additional shares of our common stock or other equity securities, and may cause our stockholders to lose part or all of their investments in our shares of common stock.

Provisions of our charter, bylaws, and Delaware law may make an acquisition of us or a change in our management more difficult.

Certain provisions of our certificate of incorporation and bylaws could discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. Stockholders who wish to participate in these transactions may not have the opportunity to do so. Furthermore, these provisions could prevent or frustrate attempts by our stockholders to replace or remove our

management. These provisions:

- allow the authorized number of directors to be changed only by resolution of our board of directors;
- establish a classified board of directors, such that not all members of the board are elected at one time;

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authorize our board of directors to issue without stockholder approval blank check preferred stock that, if issued, could operate as a poison pill to dilute the stock ownership of a potential hostile acquirer to prevent an acquisition that is not approved by our board of directors;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit stockholder action by written consent;

establish advance notice requirements for stockholder nominations to our board of directors or for stockholder proposals that can be acted on at stockholder meetings;

limit who may call stockholder meetings; and

require the approval of the holders of 80% of the outstanding shares of our capital stock entitled to vote in order to amend certain provisions of our restated certificate of incorporation and restated bylaws.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may, unless certain criteria are met, prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a prescribed period of time.

ITEM 1B. ***UNRESOLVED STAFF COMMENTS***

None.

ITEM 2. ***PROPERTIES***

As of March 6, 2009, we leased or subleased a total of approximately 166,835 square feet of office and laboratory space. The leased and subleased properties are described below:

Location	Approximate Square Footage	Use	Expiration Date
610 Lincoln Street North, Waltham, MA	85,430(1)	Laboratory and Office	9/30/18
333 Wyman Street, Waltham, MA	83,405	Office	9/30/18

(1) Under the terms of the lease for our facility at 610 Lincoln Street North, our initial leased area is approximately 63,880 square feet. Beginning in June 2009, our leased area increases to 85,430 square feet for the remainder of the lease term.

As part of our realignment plan announced on January 26, 2009, we are evaluating our options concerning future occupancy of these facilities.

ITEM 3. ***LEGAL PROCEEDINGS***

We are not currently a party to any material legal proceedings.

ITEM 4. ***SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS***

No matters were submitted to a vote of our security holders during the quarter ended December 31, 2008.

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PART II

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

Market Information

Our common stock is traded on The Nasdaq Global Market under the symbol ALTU .

The following table sets forth, for the periods indicated, the range of high and low sales prices for our common stock from January 1, 2007 through December 31, 2008:

	High	Low
2007		
First Quarter	$ 19.79	$ 13.84
Second Quarter	15.90	10.50
Third Quarter	12.21	8.47
Fourth Quarter	14.30	4.80
2008		
First Quarter	$ 7.00	$ 4.35
Second Quarter	5.67	3.65
Third Quarter	5.26	0.92
Fourth Quarter	1.18	0.44

As of March 6, 2009, there were approximately 49 holders of record and approximately 2,750 beneficial shareholders of our common stock.

Dividends

We have never paid or declared any cash dividends on our common stock and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. In addition, the terms of our redeemable preferred stock prohibit us from declaring and paying dividends on our common stock until we have paid all accrued but unpaid dividends on our redeemable preferred stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business.

Recent Sales of Unregistered Securities

None

Repurchase of Equity Securities

None

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Stock Performance Graph

We show below the cumulative total return to our stockholders during the period from January 26, 2006 (our initial public offering date) through December 31, 2008 in comparison to the cumulative return on the NASDAQ Market Index and a Peer Group Index comprised of more than 160 biotechnology companies listed on NASDAQ during the same period. The results assume that $100 was invested on January 26, 2006.

The information in this section shall not be deemed soliciting material or to be filed with the Securities and Exchange Commission, and is not to be incorporated by reference in any filing of Altus Pharmaceuticals Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K and irrespective of any general incorporation language in those filings.

COMPARISON OF 5-YEAR CUMULATIVE TOTAL RETURN
AMONG ALTUS PHARMACEUTICALS, INC.,
NASDAQ MARKET INDEX AND NASDAQ BIOTECH

ASSUMES $100 INVESTED ON JAN. 26, 2006
ASSUMES DIVIDEND REINVESTED
FISCAL YEAR ENDING DEC. 31, 2008

/26/06	03/31/06	06/30/06	09/30/06	12/31/06	03/31/07	06/30/07	09/30/07	12/31/07	03/31/08	06/3
00.00	130.38	109.69	94.95	112.07	90.49	68.61	62.37	30.80	27.05	2
00.00	103.59	93.29	97.60	99.87	86.11	100.41	106.18	100.49	97.61	9
00.00	101.40	94.65	98.43	105.50	105.86	113.83	118.06	116.00	99.39	10

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ITEM 6. ***SELECTED CONSOLIDATED FINANCIAL DATA***

The following table sets forth selected consolidated financial data for the years ended December 31, 2008, 2007, 2006, 2005 and 2004. This data, which is derived from our audited consolidated financial statements, should be read in conjunction with our audited consolidated financial statements and related notes which are included elsewhere in this Annual Report, and Management s Discussion and Analysis of Financial Condition and Results of Operations included in Item 7 below. Historical results are not necessarily indicative of operating results to be expected in the future.

	Years Ended December 31,				
	2008	2007	2006	2005	2004
	(In thousands, except per share amounts)				
Consolidated Statements of Operations Data:					
Revenue					
Contract revenue(1)	$ 2,161	$ 28,487	$ 5,107	$ 8,288	$ 4,045
Product sales(2)					185
Total revenue	2,161	28,487	5,107	8,288	4,230
Operating expenses, net					
Cost of product sales(2)					87
Research and development	83,555	70,569	50,316	26,742	19,095
General, sales and administrative	17,782	18,172	14,799	8,611	6,320
Reacquisition of European marketing rights(3) from Dr. Falk Pharma GmbH		11,493			
Gain on termination of collaboration and license agreement(1)		(4,000)			
Total operating expenses, net	101,337	96,234	65,115	35,353	25,502
Loss from operations	(99,176)	(67,747)	(60,008)	(27,065)	(21,272)
Interest income	2,921	6,683	5,022	1,018	646
Interest expense and other	(215)	(1,185)	(694)	(825)	(469)
Foreign currency exchange (loss) gain	(152)	(983)		(252)	138
Net loss	(96,622)	(63,232)	(55,680)	(27,124)	(20,957)
Preferred stock dividends and accretion	(225)	(225)	(1,286)	(10,908)	(8,588)
Net loss attributable to common stockholders	$ (96,847)	$ (63,457)	$ (56,966)	$ (38,032)	$ (29,545)
Basic and diluted net loss per share attributable to common stockholders	$ (3.13)	$ (2.23)	$ (2.75)	$ (22.13)	$ (17.33)
Shares used in computing basic and diluted net loss per share attributable to common stockholders	30,960	28,459	20,739	1,719	1,704

(1) In connection with the termination of our collaboration and license agreement with Genentech, Inc. effective December 31, 2007, in 2007 we recognized contract revenue of $25.1 million and a gain on the termination of the agreement of $4.0 million.

(2) Product sales and cost of product sales relate to the sale of crystallized enzymes for use as catalysts in pharmaceutical manufacturing processes. We stopped selling these products during the first half of 2004 and do not anticipate sales of these products in the future.

(3) In June 2007, Dr. Falk Pharma GmbH and we agreed to terminate our collaborative agreement. As part of the agreement, we agreed to pay Dr. Falk Pharma GmbH 12.0 million over a four year period. The net

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present value of this obligation was $14.1 million at then current exchange rates. This amount was immediately expensed, net of $2.7 million of remaining deferred revenue.

	As of December 31,				
	2008	2007	2006	2005	2004
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 48,600	$ 138,332	$ 85,914	$ 30,061	$ 52,638
Working capital	34,429	124,171	71,307	14,249	41,612
Total assets	64,251	154,110	96,461	40,584	62,824
Deferred revenue		2,087	8,367	13,644	10,617
Dr. Falk GmbH obligation, net of current portion(4)	4,049	6,664			
Long-term debt, net of current portion	1,432	738	2,874	3,708	3,821
Deferred rent and lease incentive obligation, net of current portion	5,645				
Redeemable preferred stock	6,731	6,506	6,281	119,373	108,465
Total stockholders equity (deficit)	29,873	119,686	69,422	(104,947)	(68,112)

(4) At the time we terminated our collaborative agreement with Dr. Falk Pharma GmbH, we recognized a liability of $14.1 million, representing the net present value of our cash payment obligation.

On January 26, 2009, we announced a strategic realignment plan to conserve capital resources, discontinue development of Trizytek and reduce headcount by approximately 75%. The financial impact of the realignment on future operating results is discussed in Management s Discussion and Analysis of Financial Condition and Results of Operations in Item 7 below.

ITEM 7. *MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS*

You should read the following discussion and analysis of financial condition and results of operations together with the Selected Consolidated Financial Data included in Item 6 above and our consolidated financial statements and related notes appearing elsewhere in this Annual Report. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this document, particularly in Item 1A above.

Overview

We are a biopharmaceutical company focused on the development and commercialization of oral and injectable protein therapeutics using our proprietary protein crystallization technology, which we believe will have significant advantages over existing products and will address unmet medical needs. Our lead product candidate is ALTU-238, a crystallized formulation of human growth hormone, for which we have completed a Phase II clinical trial in adults for growth hormone deficiency and will begin a Phase II clinical trial for growth hormone deficiency in pediatric patients in March 2009. Our next most advanced product candidate is ALTU-237, for which we have completed a Phase I clinical trial for the treatment of hyperoxalurias. We also have a pipeline of other product candidates in preclinical

research and development.

On January 31, 2006, we completed an initial public offering of 8,050,000 shares of common stock at a price of $15.00 per share. Net proceeds to us from the offering were approximately $110.2 million, net of underwriting discounts, commissions and offering expenses.

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During April 2007, we completed a common stock offering in which we sold 6,518,830 shares of common stock at a price of $14.75 per share. Net proceeds from the offering were approximately $89.9 million net of underwriting discounts, commissions and offering expenses.

We have used the net proceeds from these common stock offerings and our collaboration agreements discussed herein to fund development activities including those related to Trizytek™ (liprotamase), ALTU-238 and ALTU-237.

On January 26, 2009, we announced a strategic realignment to focus on the advancement of our long-acting, recombinant human growth hormone candidate, ALTU-238, as a once-per-week treatment for adult and pediatric patients with growth hormone deficiency. To conserve capital resources, we are discontinuing our activities in support of Trizytek, an orally delivered enzyme replacement therapy for patients suffering from malabsorption due to exocrine pancreatic insufficiency. In addition, we are evaluating the feasibility of moving forward our early-stage clinical and pre-clinical programs and will make future decisions on these programs subject to the availability of resources. In connection with the realignment, we implemented a workforce reduction of approximately 75%, primarily in functions related to the Trizytek program as well as certain general and administrative positions. As a result of these activities, we will recognize a charge of approximately $3.8 million in the first quarter of 2009 for severance and related expenses. We also anticipate further restructuring charges that could be significant due to events associated with the realignment plan, including termination of contractual obligations and facility-related costs. We expect the realignment plan will be completed in the first half of 2009.

On February 20, 2009, Cystic Fibrosis Foundation Therapeutics, Inc., or CFFTI, and we entered into a letter agreement, or the Letter Agreement, and a license agreement, or the License Agreement, terminating our strategic alliance agreement. Under the terms of the License Agreement, we assigned the Trizytek trademark and certain patent rights to CFFTI and granted CFFTI an exclusive, worldwide, royalty-bearing license to use certain other intellectual property owned or controlled by us to develop, manufacture and commercialize any product using, in any combination, the three active pharmaceutical ingredients, or APIs, which comprise Trizytek. In these agreements, we also agreed to assist CFFTI with a transition of our on-going development and regulatory activities and clinical trials through March 27, 2009, after which CFFTI will be responsible for future development activities. In exchange, CFFTI agreed to release us from all obligations and liabilities resulting from the original strategic alliance agreement, and to pay us a percentage of any proceeds CFFTI realizes associated with respect to any rights licensed or assigned to CFFTI under the License Agreement. We anticipate incurring between $8 million and $9 million in the first quarter of 2009 associated with completing specific validation activities at Lonza and continuing on-going clinical trials and NDA preparation activities through the March 27, 2009 transition.

Our future operating results will largely depend on the progress of our product candidates in the clinical development process and our ability to raise sufficient capital to fund operations. The results of our operations will vary significantly from year to year and from quarter to quarter and depend on, among other factors: our level of investment in pre-clinical and clinical research and development; our success in manufacturing drug supplies and procuring the APIs for our products; and the outcome of the clinical trials we conduct.

We have generated significant losses as we have advanced our product candidates into clinical development and expect to continue to generate losses as we continue development of ALTU-238, close out our development activities related to Trizytek and finalize our realignment of operations. As of December 31, 2008, we had $48.6 million of cash, cash equivalents and short-term marketable securities and an accumulated deficit of $335.7 million. We believe we have sufficient cash to meet our funding requirements into the fourth quarter of 2009. We will require significant additional funding to remain a going concern and to fund operations until such time, if ever, we become profitable. However, there can be no assurance that adequate additional financing will be available to us on acceptable terms.

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Financial Operations Overview

Contract Revenue. We do not expect to generate any revenue from the sale of products in the foreseeable future. Our contract revenue consists of amounts earned under former collaborative research and development agreements relating to Trizytek and ALTU-238.

In February 2001, we entered into a strategic alliance agreement with CFFTI to collaborate on the development of Trizytek and specified derivatives of Trizytek in North America for the treatment of malabsorption due to exocrine pancreatic insufficiency in patients with cystic fibrosis and other indications. The agreement, in general terms, provided us with funding from CFFTI for a portion of the development costs of Trizytek upon the achievement of specified development milestones, up to a total of $25.0 million, in return for specified payment obligations and our obligation to use good faith reasonable efforts to develop and bring Trizytek to market in North America. As of December 31, 2008, we had received a total of $18.4 million of the $25.0 million available under the CFFTI agreement, including an advance payment of $1.5 million against the final milestone payment. We were eligible to receive a final milestone payment of $6.6 million, which is net of the $1.5 million advance, less $0.2 million per annum on the advance through the date the final milestone was achieved. As noted above, on February 20, 2009, CFFTI and we entered into a series of agreements to terminate the strategic alliance agreement.

In December 2002, we entered into a development, commercialization and marketing agreement with Dr. Falk Pharma GmbH, or Dr. Falk, for the development by us of Trizytek and the commercialization by Dr. Falk of Trizytek, if approved, in Europe, the countries of the former Soviet Union, Israel and Egypt. Under the agreement, we granted Dr. Falk an exclusive, sublicensable license under specified patents to commercialize Trizytek for the treatment of symptoms caused by exocrine pancreatic insufficiency, which we refer to as the European Marketing Rights. We received upfront and milestone payments from Dr. Falk under the agreement totaling 11.0 million, which equated to $12.9 million based on exchange rates in effect at the times we received the milestone payments. Effective June 6, 2007, Dr. Falk and we agreed to terminate the agreement outside the provisions of the original agreement, and we reacquired Dr. Falk s European Marketing Rights. Under the terms of the termination agreement, we agreed to pay Dr. Falk a total of 12.0 million in installments through 2010. We will not recognize any further revenue under the agreement and will not receive any further milestone or royalty payments. At the time of the termination agreement, we recorded a net liability of $14.1 million, which reflected the net present value of our cash payment obligations to Dr. Falk. This amount was expensed in the second quarter of 2007, net of a reversal of $2.7 million of deferred revenue representing the remaining balance associated with the non-refundable upfront and milestone payments received from Dr. Falk.

In December 2006, we entered into a collaboration and license agreement with Genentech, Inc., or Genentech, for the development, manufacture and commercialization of ALTU-238. Under the terms of the agreement, we granted Genentech exclusive rights and license to make (and have made), use and import ALTU-238, and to sell ALTU-238 in North America if approved by the FDA. Genentech had the option to expand the agreement to a global agreement. The agreement, in general terms, provided that Genentech would assume full responsibility for the development, manufacture and commercialization of ALTU-238.

Pursuant to the agreement, Genentech made the following specific cash payments to us in 2007 and 2008 for work performed pursuant to the agreement:

- a $15.0 million upfront non-refundable license fee payment;