Altus Pharmaceuticals Inc.
Form 10-K
March 30, 2006

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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, 2005

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.)*
125 Sidney Street, Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	*(Zip Code)*

Registrant s telephone number, including area code:
(617) 299-2900
Securities registered pursuant to Section 12(b) of the Act:
NONE
Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $.01 par value
(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 o NO þ

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) 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, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o Accelerated filer o Non-accelerated filer þ

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 National Market on March 17, 2006 was $351,987,803. The registrant has provided this information as of March 17, 2006 because its common equity was not publicly traded as of the last business day of its most recently completed second fiscal quarter.

The number of shares outstanding of the registrant s common stock as of March 17, 2006 was 22,148,713.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive Proxy Statement to be filed in connection with the solicitation of proxies for the Annual Meeting of Stockholders to be held on July 27, 2006 are incorporated by reference into Part III of this Annual Report on 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 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 potential benefits of our product candidates over other therapies;
- the timing, costs and other limitations involved in obtaining regulatory approval for any of our product candidates;
- our ability to enter into collaboration agreements with respect to our product candidates;
- 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 ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our estimates of market sizes and anticipated uses of our product candidates;
- 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 anticipates, believes, could, estimates, expects, intends, may, plans, potential, predicts, projects, should, will, would and similar expressi 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 .

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.

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

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Biologics Inc. We have one subsidiary, Altus Pharmaceuticals Securities Corp., a Massachusetts corporation. Unless the context requires otherwise, references to Altus , we , our and us in this report refer to Altus Pharmaceuticals Inc. and our subsidiary.

Our principal executive offices are located at 125 Sidney Street, Cambridge, MA 02139, and our telephone number is (617) 299-2900. Our web site address is *www.altus.com.* The information contained on, or that can be accessed through, our web site is not incorporated by reference into this report. We have included our web site address as a factual reference and do not intend it to be an active link to our web site. 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.

Altus is a trademark of Altus Pharmaceuticals Inc. 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 and commercialization of oral and injectable protein therapeutics for gastrointestinal and metabolic disorders, with two product candidates advancing toward late stage clinical development. We are using our proprietary protein crystallization technology to develop protein therapies which we believe will have significant advantages over existing products and will address unmet medical needs. Our product candidates are designed to either increase the amount of a protein that is in short supply in the body or degrade and remove toxic metabolites from the blood stream. We have successfully completed a Phase II clinical trial of ALTU-135 for the treatment of malabsorption due to exocrine pancreatic insufficiency, and we are currently conducting a Phase II clinical trial of ALTU-238 in adults for the treatment of growth hormone deficiency. We also have a pipeline of other product candidates in preclinical research and development.

ALTU-135 for Malabsorption due to Exocrine Pancreatic Insufficiency

Our lead product candidate, ALTU-135, is an orally-administered enzyme replacement therapy consisting of three digestive enzymes, known as lipase, protease and amylase, for the treatment of malabsorption due to exocrine pancreatic insufficiency. Exocrine pancreatic insufficiency is a deficiency of digestive enzymes normally produced by the pancreas which leads to malnutrition, impaired growth and shortened life expectancy. Exocrine pancreatic insufficiency can result from a number of diseases and conditions, including cystic fibrosis, chronic pancreatitis, pancreatic cancer and HIV/AIDS. According to IMS Health, global prescription sales of existing pancreatic enzyme replacement products were $658 million in 2004.

We believe that ALTU-135, if approved, will have significant competitive advantages compared to existing pancreatic enzyme replacement therapies. We believe these potential advantages include:

- benefits associated with a drug that is microbially-derived, rather than a drug derived from pig pancreases, as is the case with existing pancreatic enzyme replacement therapies, and manufactured in a controlled environment;
- a significantly lower pill burden, allowing patients to take, on average, one capsule per meal or snack compared to, on average, four or five larger capsules per meal or snack with existing products;
- a fixed ratio of lipase, protease and amylase;
- more consistent and reliable dosing;

resistance to degradation early in the gastrointestinal tract, permitting enzyme activity where most digestion and absorption of fats, proteins and carbohydrates occurs;

the potential for a liquid formulation, which is currently unavailable with existing therapies, for children and adults who are unable to swallow capsules; and

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testing in what we believe is the largest well-controlled, scientifically rigorous, prospective clinical trial conducted to date in the treatment of cystic fibrosis patients with pancreatic insufficiency.

We believe that many of these advantages are a result of our proprietary protein crystallization technology, which enables improved product consistency and stability, as well as higher concentration and purity.

Existing pancreatic enzyme replacement products have been marketed since before enactment of the Food, Drug and Cosmetic Act, or FDCA, in 1938 and are not marketed under new drug applications, or NDAs, approved by the United States Food and Drug Administration, or FDA. In April 2004, the FDA issued a notice that manufacturers of existing pancreatic enzyme replacement products will be subject to regulatory action if they do not obtain approved NDAs for those products by April 28, 2008. We believe that some of the manufacturers of these products may not be able to satisfy the FDA s requirements for NDAs for these products.

In 2005 we completed a prospective, randomized, double-blind, dose-ranging Phase II clinical trial of the solid form of ALTU-135. In this trial, the product candidate was well tolerated and showed a statistically significant improvement in fat absorption (p-value<0.001), the trial s primary endpoint, in the two higher dose treatment arms. P-values are an indication of statistical significance reflecting the probability of an observation occurring due to chance alone. A p-value<0.001 means that the probability of the event measured occurring by chance is less than 1 in 1,000. In the two higher dose treatment arms, we also observed a statistically significant improvement in protein absorption (p-value<0.001) and a statistically significant decrease in stool weight (p-value<0.001), each of which was a secondary endpoint in the study. In addition, we observed a positive trend, although not statistically significant, in carbohydrate absorption. However, the results of our Phase II clinical trial may not be predictive of the results in our Phase III clinical trial of ALTU-135. We expect to initiate a pivotal Phase III clinical efficacy trial of the solid form of ALTU-135 in patients with cystic fibrosis and a long-term safety study in cystic fibrosis patients and other patients with pancreatic insufficiency in the second half of 2006. The FDA and the European Medicines Agency, or EMEA, have granted ALTU-135 orphan drug designation, which generally provides a drug being developed for a rare disease or condition with marketing exclusivity for seven years in the United States and 10 years in the European Union if it is the first drug of its type approved for such indication. Additionally, the FDA has granted ALTU-135 fast track designation and admission into its Continuous Marketing Application, or CMA, Pilot 2 Program, both of which are designed to facilitate interactions between a drug developer and the FDA during the drug development process.

ALTU-238 for Growth Hormone Deficiency and Related Disorders

Our next most advanced product candidate, 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 and hGH-related disorders. Based on reported revenues of existing products, global sales of hGH products exceeded $2.2 billion in 2004, and the market grew at a compound annual growth rate of approximately 15% from 2002 to 2004. 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 our Phase I clinical trial of ALTU-238, which we completed in May 2005, ALTU-238 demonstrated pharmacokinetic and pharmacodynamic parameters that are consistent with once-weekly administration. We believe that the convenience of once-weekly administration of ALTU-238, if approved, would improve patient acceptance and compliance, and thereby effectiveness. We are conducting a Phase II clinical trial for ALTU-238 in adults with growth hormone deficiency and expect to have data from this trial in the first half of 2006.

Pipeline and Technology

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. Our most advanced preclinical product candidates are ALTU-237, designed to treat hyperoxalurias, and ALTU-236, designed to

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treat phenylketonuria. We believe that these product candidates, if approved, will provide treatments for these disorders, both of which lack any approved pharmaceutical therapies. We expect to file an investigational new drug application, or IND, for ALTU-237 for the treatment of hyperoxalurias in early 2007.

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, our product candidate ALTU-135 is based on known enzymes to which we apply our proprietary crystallization technology with the goal of offering a new and improved drug. We have developed 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 solid and liquid oral form, as well as in extended-release injectable formulations. Our product candidates are designed to offer improvements over existing products, such as greater convenience, better safety and efficacy 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.

We currently hold worldwide rights to all of our product candidates, except for rights we have licensed to Dr. Falk Pharma GmbH, or Dr. Falk, a specialty pharma company headquartered in Germany, to commercialize ALTU-135 in Europe, the countries of the former Soviet Union, Israel and Egypt. We have also entered into a strategic alliance agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFTI, which is funding a portion of the development of ALTU-135. We intend to establish a commercial infrastructure and a targeted specialty sales force to market our products in North America.

Our Strategy

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

Focus on advancing our lead product candidates. We have two product candidates advancing toward late stage clinical trials. We are preparing ALTU-135 for a pivotal Phase III clinical trial for the treatment of malabsorption due to exocrine pancreatic insufficiency. In addition, we are conducting a Phase II clinical trial of ALTU-238 in adult growth hormone deficient patients. If this trial is successful, we plan to initiate a Phase III clinical trial in adults and a Phase II/III clinical trial in pediatric patients, which we plan to request that the FDA consider to be a pivotal trial. However, the FDA may not agree with our proposed combined Phase II/III clinical trial in pediatric patients and may require additional studies in children. We believe that these product candidates, if approved, will offer significant advantages over existing therapies. In addition, because these product candidates are based on well-understood proteins with known mechanisms of action, we believe we may be able to reduce their development risk and time to market. Our primary focus is on aggressively advancing the clinical development of these two product candidates to NDA submission.

Continue to build and advance our product pipeline for gastrointestinal and metabolic disorders. In addition to our product candidates in clinical development, we have built a pipeline of preclinical product candidates based on our proprietary protein crystallization technology. These product candidates are designed to address unmet needs for the treatment of hyperoxalurias, phenylketonuria, and other gastrointestinal and metabolic diseases. We plan to apply the manufacturing, clinical and regulatory experience gained from our two lead product candidates to advance a number of these preclinical product candidates into clinical trials over the next few

years. We also plan to add additional product candidates to our pipeline through the application of our proprietary protein crystallization technology to existing protein therapeutics or known proteins with potential therapeutic use.

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Establish a commercial infrastructure. We plan to establish a commercial infrastructure and targeted specialty sales force to market our two lead product candidates in North America. In addition, we plan to leverage our sales and marketing capabilities by targeting the same groups of physician specialists with additional products that we bring to market either through our own development efforts or by in-licensing from others.

Selectively establish collaborations for our product candidates with leading pharmaceutical and biotechnology companies. We currently have a collaboration with Dr. Falk for the commercialization of ALTU-135 in Europe, the countries of the former Soviet Union, Israel and Egypt. We intend to develop additional collaborations in markets outside of North America where we believe that having a collaborator will enable us to gain better access to those markets. We may also collaborate with other companies to accelerate the development of some of our early-stage product candidates, to co-commercialize our product candidates in North America in instances where we believe that a larger sales and marketing presence will expand the market or accelerate penetration, or to advance other business objectives.

Establish additional collaborations to apply our technology to other therapeutic proteins. We believe that our technology has broad applicability to many classes of 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

The following table summarizes key information about our product candidates that are in clinical trials and our most advanced preclinical research and development programs. All of the product candidates are based on our crystallization technology and are the result of our internal research and development efforts.

Product Candidate (Delivery) Indication	Stage of Development	Commercial Rights	Status
ALTU-135 (oral) *Exocrine Pancreatic Insufficiency*	Phase II completed	Dr. Falk (Europe, the countries of the former Soviet Union, Israel and Egypt)	Phase III clinical efficacy trial and long-term safety study of the solid form expected to begin in the second half of 2006; Phase II clinical trial of the liquid form expected to begin in early 2007
		Altus (United States and rest of world)	
ALTU-238 (injectable) *Growth Disorders*	Phase II	Altus	Data from Phase II clinical trial in adults expected in the first half of 2006; Phase III clinical trial in adults and Phase II/III clinical trial in children expected to

			begin in the second half of 2006
ALTU-237 (oral) *Hyperoxalurias*	Preclinical	Altus	IND enabling work in progress, with IND filing expected in early 2007
ALTU-236 (oral) *Phenylketonuria*	Preclinical	Altus	Preclinical testing in animal models

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We may be required to perform additional studies in order to obtain marketing approval for ALTU-135 and ALTU-238 even if the clinical trials we currently expect to conduct are successful. In addition, if the FDA does not agree with our proposed combined Phase II/III clinical trial of ALTU-238 in children, we may be required to conduct additional studies in children.

We are developing our product candidates with the goal of initially seeking marketing approvals in the United States and the European Union. In addition to our regulatory activities for ALTU-135 in the U.S., we and Dr. Falk have agreed with the EMEA on our pre-clinical plan and are in discussions with the EMEA for our clinical plan. For ALTU-238, we plan to submit an initial request for guidance on regulatory matters from European regulatory authorities during the second half of 2006. We expect that the data from the studies we have conducted or plan to conduct pursuant to the INDs for ALTU-135 and ALTU-238 we have filed with the FDA will form a substantial part of the applications for marketing approval to be filed with the EMEA and regulatory authorities in other parts of the world. However, we may be required to perform additional clinical trials to receive marketing approval outside the United States.

ALTU-135 for Exocrine Pancreatic Insufficiency

Our lead product candidate, ALTU-135, is an orally administered enzyme replacement therapy for which we have successfully completed a Phase II clinical trial of its solid form for the treatment of malabsorption due to 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. Conditions resulting in exocrine pancreatic insufficiency include cystic fibrosis, chronic pancreatitis, pancreatic cancer and HIV/AIDS. Patients with exocrine pancreatic insufficiency are currently treated with enzyme replacement products containing enzymes derived from pig pancreases. We believe that ALTU-135 represents a significant potential advancement as a therapeutic alternative for the treatment of these patients.

ALTU-135 contains three types of digestive enzymes derived from non-animal sources:

Lipase. We selected the lipase in ALTU-135, which is used for the digestion of fats, because it demonstrated the ability in *in vitro* and animal testing to be active across a wide range of acidity levels and more resistant to degradation in the harsh environment of the gastrointestinal tract when compared to other lipases. It also demonstrated the ability to break down a broader range of fats than existing animal-derived lipases. Because lipases are the most susceptible of the three enzymes to degradation in the gastrointestinal tract, we use our proprietary technology to both crystallize and cross-link the lipase for increased activity and stability;

Protease. We selected the protease in ALTU-135, which is used for the digestion of proteins, because it demonstrated the ability in *in vitro* and animal testing to break down as many types of proteins as the multiple proteases contained in existing products. We crystallize the protease for greater stability and concentration; and

Amylase. We selected the amylase in ALTU-135, which is used for the digestion of carbohydrates, because it demonstrated the ability in *in vitro* testing to be active in the highly acidic environment of the upper gastrointestinal tract. Because the amylase is stable in soluble form, we do not crystallize it.

Our contract manufacturer produces these enzymes from microbial sources using separate fermentation and purification processes. The enzymes are then blended to achieve a specified and consistent ratio of lipase to protease to amylase in each capsule.

Disease Background and Market Opportunity

We have designed ALTU-135 to treat malabsorption resulting from exocrine pancreatic insufficiency. Malabsorption is the failure to absorb adequate amounts of nutrients, such as fats, proteins and carbohydrates, in food and is clinically manifested as malnutrition, weight loss or poor weight gain, impaired growth, abdominal bloating, cramping and chronic diarrhea. Exocrine pancreatic insufficiency is a deficiency of digestive enzymes normally produced by the pancreas that results in poor absorption of essential nutrients

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from food. If not treated appropriately, exocrine pancreatic insufficiency generally leads to malnutrition, impaired growth and shortened life expectancy.

According to IMS Health, the worldwide market for pancreatic enzyme replacement therapies grew at a compound annual growth rate of approximately 7% from $579 million in 2002 to $658 million in 2004. The market for these products in 2004 was approximately $190 million in North America, $228 million in Europe and $241 million in the rest of the world according to IMS Health. Diseases and conditions with a prevalence of exocrine pancreatic insufficiency include:

Cystic fibrosis Cystic fibrosis is one of the most prevalent genetic disorders in the Caucasian population, according to the Medical Genetics Institute of Cedars-Sinai. According to the Cystic Fibrosis Foundation, this disease affects approximately 30,000 people in the United States. Approximately 90% of cystic fibrosis patients are prescribed pancreatic enzymes to treat exocrine pancreatic insufficiency. Cystic fibrosis patients with exocrine pancreatic insufficiency have a median life expectancy of 31 years, compared to 50 years for those cystic fibrosis patients who have sufficient pancreatic enzymes.

Chronic pancreatitis In many patients, chronic pancreatitis is clinically silent and many patients with unexplained abdominal pain may have chronic pancreatitis that eludes diagnosis. As a result, according to The New England Journal of Medicine, the true prevalence of the disease is not known, although estimates range from 0.04% to 5% of the United States population. Based on survey data reported in Medscape General Medicine, we believe chronic pancreatitis results in more than 500,000 physician visits per year in the United States.

Pancreatic cancer The American Cancer Society estimates that approximately 30,000 people in the United States are diagnosed with pancreatic cancer each year. According to an industry estimate, approximately 65% of patients with pancreatic cancer will have some degree of fat malabsorption.

HIV/AIDS According to the U.S. Centers for Disease Control and Prevention, there were approximately 1.1 million people with HIV/AIDS in the United States in 2003. Approximately 50% of HIV-positive patients in an industry study had evidence of pancreatic insufficiency.

Limitations of Existing Products

Patients with exocrine pancreatic insufficiency are typically prescribed enzyme replacement products containing enzymes extracted from pig pancreases. Many of these products were available for human use prior to the passage of the FDCA in 1938, and all are currently marketed without NDAs approved by the FDA. In 1995, the FDA issued a final rule requiring that these pancreatic enzyme products be marketed by prescription only, and in April 2004, the FDA issued a notice that manufacturers of these products will be subject to regulatory action if they do not obtain approved NDAs for these products by April 28, 2008. At the same time, the FDA also issued draft guidance, known as the PEP Guidance, that existing manufacturers of pancreatic enzyme products can follow in order to obtain FDA approval.

Existing pancreatic enzyme replacement therapies are derived from pig pancreases and are supposed to be taken with every meal and snack in order to permit the digestion and absorption by the patient of sufficient amounts of fats, proteins and carbohydrates. We believe that these products have a number of significant limitations that affect their ease of administration, safety and effectiveness, including:

High pill burden. Patients on existing pancreatic enzyme therapies are generally required to take, on average, four or five larger capsules per meal or snack, resulting in poor compliance and therefore reduced long-term

efficacy, due to the following factors:

Degradation of enzymes in the gastrointestinal tract. A significant portion of the enzymes in existing products are degraded in the gastrointestinal tract prior to exerting their therapeutic effect. As a result, many patients are required to take many capsules to achieve a desired level of absorption of fats, proteins and carbohydrates. Some manufacturers have tried to address this issue by adding a protective coating to the enzymes, but this often results in a failure of the enzyme to dissolve and

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become active early enough in the gastrointestinal tract to break down foods and effectively assist with the digestive process.

Low concentration. Existing therapies are comprised of a mixture of enzymes and other materials found in a pig s pancreas. Based on comments submitted in response to the FDA s PEP Guidance in 2004 by manufacturers of existing products and the components of such products, we believe that manufacturers of these products are unable to concentrate the enzymes in the mixture to reduce the amount of material a patient must consume.

Variability of therapeutic effect. Because existing products are extracted from pig pancreases, there is significant variability between different manufacturing batches. As a result, we believe that the therapeutic effect of these therapies is also significantly variable. Each time a patient refills a prescription, the patient may need to experiment with the number of pills taken per meal or snack to achieve effective digestion of his or her food intake.

Short shelf life. Existing enzyme therapies tend to lose activity quickly relative to other types of drugs. Many manufacturers try to overcome this limitation by filling each capsule with more drug than specified in order to achieve the stated label claim over time, which leads to inconsistent efficacy and raises safety concerns. We believe this also contributes to patient uncertainty about the number of capsules to take per meal or snack.

Product impurities. Existing enzyme therapies are poorly characterized and may contain impurities, including porcine viruses, tissue components and other contaminants. These impurities may increase the risk of antigenicity, or an immune system reaction.

Anticipated Advantages of ALTU-135

We believe that ALTU-135, if approved, will offer patients a more convenient and effective long-term therapy for the treatment of malabsorption due to exocrine pancreatic insufficiency because of the following features:

Reduced pill burden. ALTU-135 is a highly concentrated, pure and stable enzyme replacement therapy designed to be as effective as existing products with significantly fewer capsules. Based on the clinical trials we have conducted to date, we believe that most patients will be effectively treated with, on average, one capsule per meal or snack. We believe that this dosing will result in greater convenience for the patient, which will improve compliance and, therefore, long-term effectiveness of therapy. We believe that ALTU-135 will reduce the pill burden for patients due to the following factors:

Stability of enzymes in the gastrointestinal tract. We have designed ALTU-135 to withstand degradation, maintain its activity across the different pH levels in the gastrointestinal tract, and exert its therapeutic effect in the first part of the small intestine, or the duodenum, where most fats, proteins and carbohydrates are broken down and absorbed. We believe this design will provide a more effective treatment for patients than current pancreatic enzyme replacement products, which are often degraded earlier in the gastrointestinal tract.

High concentration. Two of the three enzymes in ALTU-135 are crystallized, resulting in a highly concentrated product that requires less material to achieve a desired therapeutic effect.

Consistent activity. We have designed ALTU-135 to exhibit consistent enzyme activity from batch to batch. The enzymes in ALTU-135 are microbially derived and produced through fermentation. The amount of material and related enzyme activity in a capsule of ALTU-135 is tightly controlled, as each of the three enzymes in ALTU-135 is individually manufactured and added to the final drug product in a specific amount. We believe

this will result in consistent product performance, eliminating the need for dose experimentation each time a patient refills a prescription.

Longer shelf life. Based on stability studies performed as part of our development program, we believe that ALTU-135 capsules are significantly more stable than existing porcine-derived products, which we expect will lead to a longer effective shelf life and more reliable and consistent dosing.

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Potential liquid formulation. We have completed *in vivo* studies of a liquid formulation of ALTU-135. We believe that a liquid formulation will significantly benefit children and adults who are unable to swallow capsules.

ALTU-135 Development Activities and Strategy

We have successfully completed a Phase II clinical trial of the solid form of ALTU-135 and are preparing to advance this product candidate into a pivotal Phase III clinical efficacy trial in patients with cystic fibrosis and a long-term safety study in cystic fibrosis patients and other patients with pancreatic insufficiency in the second half of 2006. The FDA and the EMEA have granted ALTU-135 orphan drug designation for malabsorption due to exocrine pancreatic insufficiency, and the FDA has also granted ALTU-135 fast track designation. Fast track designation is designed to facilitate the development of new drugs and may be granted to a product with a specific indication where the FDA agrees that the product is intended to treat a serious or life threatening condition and demonstrates the potential to address unmet medical needs for that condition. Fast track designation also permits drug developers to submit sections of an NDA as they become available. In February 2004, ALTU-135 was also admitted to the FDA s CMA Pilot 2 Program. Under the CMA Pilot 2 program, one fast track designated product from each review division of the Center for Drug Evaluation and Research, or CDER, the center at the FDA that regulates drugs and therapeutic biologics, and the Center for Biologics Evaluation and Research, or CBER, the center at the FDA that regulates other biologics, is selected for frequent scientific feedback and interactions with the FDA, with a goal of improving the efficiency and effectiveness of the drug development process. We plan to submit our NDA for ALTU-135 to the FDA in 2007.

We have completed four clinical trials of ALTU-135, three of which were in cystic fibrosis patients and one of which was in healthy volunteers. The following table summarizes the clinical trials of ALTU-135 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

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 and Phase II clinical trials, we also measured the number and weight of the patients stools.

Phase I Clinical Trials

In our three Phase I clinical trials, the solid form of ALTU-135 was generally well tolerated at doses of up to four times the recommended clinical dose. In addition, in our Phase Ib trial, we observed statistically significant evidence of clinical activity based on CFA, CNA and stool results when all cohorts in the Phase Ib were considered together. In the Phase Ic trial, we observed evidence of amylase activity based on a treatment-associated increase in maximum

glucose levels in a small number of subjects.

Phase II Clinical Trial

We successfully completed our Phase II clinical trial for ALTU-135 and presented the results of the trial at the North American Cystic Fibrosis Conference in October 2005. In the trial, ALTU-135 was well tolerated

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and showed a statistically significant improvement in fat absorption (p-value<0.001), the trial s primary endpoint, in the two higher dose treatment arms. In these treatment arms, we also observed a statistically significant improvement in protein absorption (p-value<0.001) and a statistically significant decrease in stool weight (p-value<0.001), each of which was a secondary endpoint in the study. In addition, we observed a positive trend, although not statistically significant, in carbohydrate absorption in these treatment arms.

We believe that this is the first clinical trial to demonstrate that the combination of the three enzymes in ALTU-135, lipase, protease and amylase, may be effective in treating pancreatic insufficiency. We also believe that this trial is the only trial to concurrently evaluate the impact of a fixed dose of enzyme replacement therapy on the absorption of fats, proteins and carbohydrates. Based on the results from our Phase II clinical trial and earlier trials for ALTU-135, we believe that:

a formulation of ALTU-135 consisting of 25,000 units of lipase, 25,000 units of protease and 3,750 units of amylase, representing a ratio of 1:1:0.15, is the minimal dose combination that provides a clinically meaningful improvement in fat and protein absorption;

most patients will be able to be treated with one small capsule of ALTU-135 per meal or snack; and

patients with the most severe fat and protein malabsorption will realize the greatest benefit from treatment with ALTU-135.

Study Design and Demographics

The purpose of our Phase II clinical trial of ALTU-135 was to obtain initial efficacy data, select a dose level of ALTU-135 for further evaluation in our Phase III clinical trial and assess the safety and tolerability of ALTU-135 over a 28-day treatment period in cystic fibrosis patients with pancreatic insufficiency. We believe our Phase II clinical trial of ALTU-135 represents the largest prospective, randomized, double-blind, dose-ranging trial conducted to date in the treatment of cystic fibrosis patients with pancreatic insufficiency.

To establish a baseline period measurement of fat, protein and carbohydrate absorption, at the beginning of the trial patients were tested during a 72-hour period when they were not taking enzyme replacement therapy. Following this baseline period, ALTU-135 in capsule form was orally administered to patients with each of five meals or snacks per day for a period of 28 days. In the middle of the trial, we performed an additional measurement of fat, protein and carbohydrate absorption to establish these measurements for the treatment period. For both the baseline and treatment period measurements, we assessed fat and protein absorption following a 72-hour, controlled, high-fat diet by examining stools collected from patients. The appropriate period for measuring fat and protein absorption was determined by using a blue dye stool marker, which facilitated accurate and complete stool collection. Changes in carbohydrate absorption were determined by measuring blood glucose responses using the starch challenge test. We assessed the clinical activity of the lipase component of ALTU-135 by measuring the change in CFA, the clinical activity of the protease component of ALTU-135 by measuring the change in CNA and the clinical activity of the amylase component of ALTU-135 by measuring the change in carbohydrate absorption.

The Phase II clinical trial for ALTU-135 enrolled a total of 129 subjects with cystic fibrosis and pancreatic insufficiency in 26 cystic fibrosis centers in the United States. The demographics and baseline characteristics of the patients in the trial generally reflect the cystic fibrosis patient population. Ninety-five percent of the patients in the trial were Caucasian. The trial consisted of patients between the ages of 11 and 55, with a median age of 21.

The study included three treatment arms of approximately equal size, with patients in each arm receiving a fixed dose of ALTU-135 in capsule form administered orally:

Treatment arm 1 5,000 units lipase: 5,000 units protease: 750 units amylase per meal or snack;

Treatment arm 2 25,000 units lipase: 25,000 units protease: 3,750 units amylase per meal or snack, which is the dose we have selected to use in our planned Phase III clinical trials; and

Treatment arm 3 100,000 units lipase: 100,000 units protease: 15,000 units amylase per meal or snack.

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The trial did not include a placebo arm, as we assessed efficacy based on the differences in fat, protein and carbohydrate absorption between the baseline period and the treatment period.

Efficacy Results

Of the 129 patients who were enrolled in the trial, 117 patients had valid stool collections during the ALTU-135 treatment period. We used this subset of patients for our main efficacy analyses. The results of the Phase II clinical trial showed a statistically significant improvement in CFA from the baseline period to the treatment period (p-value<0.001) for patients in treatment arms 2 and 3. The results of the trial also showed a statistically significant difference between on-treatment CFAs for patients in treatment arms 2 and 3 relative to treatment arm 1; therefore, the trial achieved its primary efficacy endpoint. We also observed a statistically significant improvement in CNA from the baseline period to the treatment period (p-value<0.001) and a statistically significant decrease in stool weight from the baseline period to the treatment period (p-value<0.001) for patients in treatment arms 2 and 3. The trial results also indicated a trend, although not statistically significant, toward improvement in carbohydrate absorption for patients in treatment arms 2 and 3.

We also observed statistically significant improvements in CNA from the baseline period to the treatment period for patients in treatment arms 2 and 3, as compared to patients in treatment arm 1. In addition, changes in CFA and CNA were highly correlated (r=0.844, p-value<0.001), supporting the 1:1 ratio of the units of lipase and protease in the formulation. The correlation coefficient, r, is the measure of correlation between two sets of data. Based on the results of our Phase II clinical trial, we have selected a formulation of ALTU-135 consisting of 25,000 units of lipase, 25,000 units of protease and 3,750 units of amylase as the dose level for testing in our proposed Phase III clinical trial.

In treatment arm 2 there was an average 11.4 percentage point increase in CFA, from 55.6% to 67.0%, and an average 12.5 percentage point increase in CNA, from 58.8% to 71.3%, from the baseline period to the treatment period. In treatment arm 3 there was an average 17.3 percentage point increase in CFA, from 52.2% to 69.7%, and an average 17.5 percentage point increase in CNA, from 56.8% to 74.6%, from the baseline period to the treatment period. There was not a statistically significant difference between these results. Based on these increases in CFA and CNA, we believe that cystic fibrosis patients suffering from malabsorption who are treated with ALTU-135 may experience clinically meaningful improvements in fat and protein absorption, resulting in an overall improvement in nutritional status. We also believe that an improvement in nutritional status may lead to weight maintenance or weight gain in patients, both of which are important elements in the overall health of cystic fibrosis patients and others suffering from pancreatic insufficiency. According to the Cystic Fibrosis Foundation 2003 Patient Registry, more than 90% of cystic fibrosis patients take currently available pancreatic enzyme replacement therapies and approximately 35% of cystic fibrosis patients are in urgent need of improved nutrition.

We believe that an improvement in CFA of 10 percentage points or more represents a clinically meaningful benefit to patients with pancreatic insufficiency. Clinicians who treat cystic fibrosis patients typically recommend a high fat diet consistent with the diet in our Phase II clinical trial. Patients in our Phase II clinical trial consumed, on average, 100 grams of fat per day. In these patients, an average increase in fat absorption of 10 percentage points would equate to 10 grams of additional fat absorbed per day. According to the FDA, there are nine calories in a gram of fat. As a result, an improvement in CFA of 10 percentage points would equate to an additional 90 calories absorbed per day. Over a period of one year, such a 90 calorie per day increase would result in an improvement in weight of approximately nine pounds, allowing patients to either maintain weight that they may have otherwise lost or gain weight.

To gain a better understanding of the clinical impact of treatment with ALTU-135, we further analyzed the data on CFA and CNA improvements in our Phase II clinical trial, specifically focusing on differences experienced by

patients who began the trial with lower levels of fat and protein absorption during the baseline period, as compared with patients who began the trial with higher baseline levels of fat and protein absorption. We examined two groups: patients who absorbed 40% or less of their fat or protein intake during the baseline period, and patients who absorbed more than 40% of their fat or protein intake during the baseline period. In this retrospective analysis, we looked only at data from patients in treatment arms 2 and 3, and we pooled

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these two groups for purposes of the analysis, as there were no statistically significant differences between these treatment arms in improvements in CFA and CNA.

When we analyzed those patients who absorbed 40% or less of their fat or protein intake during the baseline period we observed the following results:

- an average increase in CFA of 31 percentage points for combined treatment arms 2 and 3, from the baseline period to the treatment period (number of patients, or n=21)

- an average increase in CNA of 36 percentage points for combined treatment arms 2 and 3, from the baseline period to the treatment period (n=9)

In patients with fat or protein absorption of between 40% and 80% during the baseline period, we observed the following results:

- an average increase in CFA of 9 percentage points for combined treatment arms 2 and 3, from the baseline period to the treatment period (n=50)

- an average increase in CNA of 13 percentage points for combined treatment arms 2 and 3, from the baseline period to the treatment period (n=60)

Based on these data, we believe cystic fibrosis patients enrolled in our Phase II clinical trial had a clinically meaningful response to ALTU-135. In particular, those subjects who had the most severe fat or protein malabsorption, which we define as patients with a CFA or CNA of 40% or less during the baseline period, benefited the most from their treatment with ALTU-135. Based on our discussions with the FDA to date, we expect that in our Phase III clinical trial of ALTU-135, the FDA will look for ALTU-135 to provide patients who have a lower baseline CFA level a substantially greater percentage point increase in CFA than the percentage point increase in patients who have a higher baseline CFA level in order to demonstrate clinically meaningful improvement.

As noted above, the trial results also indicated a trend toward improvement in carbohydrate absorption for patients in treatment arms 2 and 3. To obtain additional insight with respect to carbohydrate absorption, we further analyzed the data retrospectively by examining all three treatment arms using a responder analysis that excluded subjects with cystic fibrosis-related diabetes, because those subjects were receiving diabetes medications that could have confounded the results. In this subgroup (n=81), we observed a marked increase in the number of subjects whom we considered responders in treatment arms 2 and 3 compared to treatment arm 1. We defined responders as patients who achieved a minimum predetermined level of glucose change during the treatment period as compared to the pre-treatment period. The number of subjects achieving this response in treatment arm 2 was statistically significant when compared to treatment arm 1 (p-value<0.01) and was approaching statistical significance for treatment arm 3 (p-value=0.0644) compared to treatment arm 1.

Safety and Tolerability Results

There were no statistically significant differences among the three treatment arms in the incidence of adverse events, or AEs, the number of related AEs, or the number of serious adverse events, or SAEs. The majority of AEs were mild in intensity, similar to previous ALTU-135 studies in cystic fibrosis subjects, and the most frequently reported AEs were gastrointestinal disorders. There were no clear differences across the treatment arms for any AEs considered to be related to ALTU-135. The majority of the SAEs were gastrointestinal and pulmonary related, which were consistent with the subjects underlying cystic fibrosis disease. Of the SAEs, only one was considered by an investigator in the trial as probably or possibly related to treatment with ALTU-135.

There were no major safety concerns identified regarding laboratory values, vital signs or physical exams. Abnormal liver transaminase values with frequent fluctuations were common among the subjects during the pre-treatment, treatment and follow-up periods, and are common in the cystic fibrosis population in general. We observed, however, more frequent liver transaminase elevations in subjects during the treatment and follow-up periods compared to the pre-treatment period. In a 1999 published study of 124 children with cystic

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fibrosis who were followed for four years, it was found that 80% had abnormal elevations in liver transaminases. Overall transaminase elevations experienced by patients in our Phase II trial were transient, asymptomatic and not associated with increases in bilirubin. Increases in bilirubin are typically associated with harm to the liver. In addition to normal to abnormal transaminase shifts, abnormal to normal transaminase shifts were also observed across treatment groups. A causal relationship between ALTU-135 treatment and elevated liver transaminases is unclear because of the underlying liver disease, which is estimated to occur in up to 37% of cystic fibrosis patients according to published studies, and other complicating factors in these patients, including diabetes and infections.

Phase III Clinical Trial in Cystic Fibrosis Patients

We have met with the FDA to discuss the results of our Phase II clinical trial and had discussions with the FDA about our planned Phase III clinical trial for the solid form of ALTU-135. Based on our discussions with the FDA to date, we are currently designing our pivotal Phase III clinical trial of ALTU-135 to be a multicenter, randomized, double-blind, placebo-controlled clinical study to determine, as the primary endpoint, the efficacy of ALTU-135 in the treatment of fat malabsorption in cystic fibrosis patients with exocrine pancreatic insufficiency through measurement of CFA. We plan to incorporate secondary endpoints in the study, including the evaluation of ALTU-135 in the treatment of protein and carbohydrate absorption through measurement of CNA and use of the starch challenge test, and in decreasing the weight of stools in patients. In the trial, we also plan to evaluate the safety and tolerability of ALTU-135 for approximately two months. Our current draft protocol contemplates the enrollment of approximately 150 cystic fibrosis patients over the age of seven with exocrine pancreatic insufficiency at cystic fibrosis centers in the United States, Canada and Europe. Patients will take one small capsule of ALTU-135 containing 25,000 units of lipase, 25,000 units of protease and 3,750 units of amylase with each meal or snack. The protocol is not finalized and may change as a result of our ongoing discussions with the FDA. We are preparing to initiate the Phase III clinical efficacy trial of the solid form of ALTU-135 in the second half of 2006 in cystic fibrosis patients and expect to complete the clinical testing in this trial in the first half of 2007.

Long-Term Safety Study

We are planning to initiate a clinical study evaluating the long-term safety of ALTU-135 in the treatment of cystic fibrosis and other patients with exocrine pancreatic insufficiency in the second half of 2006. This study will evaluate the safety of ALTU-135 following one year of open-label treatment in order to provide the necessary six-month and 12-month exposure data for approval of an NDA. We plan to enroll approximately 250 patients with pancreatic insufficiency from a combination of sources, including our Phase II and Phase III clinical trials of ALTU-135. The safety of ALTU-135 will be evaluated based on adverse events, physical examinations, vital signs and standard clinical laboratory testing during the one-year study period.

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 disorders in both pediatric and adult populations. Based on reported revenues of existing products, these indications generated approximately $2.2 billion in worldwide sales of hGH in 2004, and the market grew at a compound annual growth rate of approximately 15% from 2002 to 2004. We are developing ALTU-238 as a long-acting, growth hormone product that can allow patients to avoid the inconvenience of daily injections as 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 molecule with an established record of 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 completed a Phase I clinical trial of ALTU-238 in healthy adults that was designed to determine its safety, pharmacokinetics and pharmacodynamics. 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. Based on the results of our Phase I clinical trial, we have initiated a

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Phase II clinical trial for ALTU-238 in adults with growth hormone deficiency and expect to have data from this trial in the first half of 2006.

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. 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. Growth hormone also 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 the pituitary gland that impairs its ability 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, in adults low levels of hGH are also frequently associated with other metabolic disorders, including lipid abnormalities, decreased bone density, obesity, insulin resistance, decreased cardiac performance and decreased muscle mass. These disorders typically become increasingly apparent after a prolonged period of hGH deficiency, as occurs in adulthood.

Patients with growth hormone deficiency are typically treated with growth hormone replacement therapy. Growth hormone is also prescribed for many patients suffering from a range of other diseases or disorders, including pediatric growth hormone deficiency, adult growth hormone deficiency, 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, HIV/AIDS wasting, Prader Willi Syndrome 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 eight FDA-approved hGH products on the market in the United States from six 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.

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 many of those who do fail to continue treatment.

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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 clinical trial, we believe that ALTU-238 will offer growth hormone deficient patients the convenience of a once-weekly injection. We believe this will improve 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 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 prolonged injection time, which we believe led to reduced market acceptance and eventual withdrawal of the product from the market. 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 a Phase I clinical trial of ALTU-238 in healthy adults and are conducting a Phase II clinical trial in adults with growth hormone deficiency. We expect to have data from this trial in the first half of 2006.

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Phase I Clinical Trial

In our Phase I clinical trial, we evaluated the safety, tolerability and the pharmacokinetic and pharmacodynamic profile of ALTU-238 in healthy adults. The following is a summary of our Phase I clinical trial for ALTU-238:

ALTU-238 Phase I Clinical Trial Summary

Title	A Single Blind, Single Dose, Randomized, Placebo-Controlled, Parallel Group Study of ALTU-238 in Normal Healthy Adults to Determine Pharmacokinetics, Pharmacodynamics and Drug Safety.
Design	Forty-five subjects received one of the following treatment regimens: a single injection of ALTU-238 at a dose of 2.8 mg, 8.4 mg, or 16.8 mg of hGH, administered to 6 subjects at each dose; a single injection of ALTU-238 at a dose of 24.5 mg of hGH administered to 7 subjects; 7 daily injections of Nutropin AQ, a daily, FDA-approved hGH product, at a dose of 2.4 mg of hGH, administered to 6 subjects; a single injection of Nutropin AQ at a dose of 3.5 mg of hGH, administered to 6 subjects; and a single injection of placebo, administered to 8 subjects.
Administration	Each regimen was administered to patients as a subcutaneous injection.
Safety Results	ALTU-238 was well tolerated and easily administered through 29 and 30 gauge needles. 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 experienced injection site reactions, the most common of which were redness, hardening of the skin and swelling.
Clinical Activity Results	We observed a dose-dependent rise in hGH and IGF-1 concentrations following a single dose of ALTU-238. The pharmacokinetic profile of ALTU-238 at a dose of 16.8 mg indicated that the maximum concentration of hGH in the blood was achieved in approximately 51 hours and was less than the maximum concentration of hGH in the blood from a daily dose of 2.4 mg of Nutropin AQ. The IGF-1 pharmacodynamic profile over a seven-day period after a single injection of ALTU-238 at a dose of 16.8 mg was comparable to that observed with the same aggregate amount of hGH delivered through seven daily injections of Nutropin AQ.

Based on the results from the Phase I clinical trial, we believe that ALTU-238, if approved, can be administered once weekly.

Phase II Clinical Trial

In our Phase II clinical trial, we are evaluating ALTU-238 in adults with growth hormone deficiency. The primary objective of the trial is 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 clinical trial consists of two treatment groups of at least six patients each. Patients will receive weekly injections of either 5.6 mg or 11.2 mg of ALTU-238, which we believe are consistent with the doses for adult and pediatric indications. We will determine the pharmacokinetic and pharmacodynamic profiles of ALTU-238 by measuring hGH, IGF-1 and other parameters in 10 evaluable patients. We expect to have data from this trial in the first half of 2006. If our Phase II clinical trial is successful, we plan to advance ALTU-238 into a Phase III clinical trial in adults and a Phase II/III clinical trial in

children in the second half of 2006. We plan to request that the FDA consider the single trial in children as a pivotal trial because we are designing the trial to meet the requirements of both a Phase II and Phase III trial. The FDA may not agree with this approach and may require additional studies in children.

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Our current plan is to file a full NDA for ALTU-238 under section 505(b)(1) of the FDCA. We have reached agreement on the necessary non-clinical studies and plan to discuss our clinical program with the FDA after we complete our Phase II study in growth hormone deficient adults.

Our Preclinical Research and Development Programs

We are currently developing a pipeline of preclinical product candidates that are designed to either increase the amount of protein that is in short supply in the body or degrade and remove toxic metabolites from the blood stream. We are developing all of these product candidates for oral delivery to address areas of unmet need in gastrointestinal and metabolic disorders, including: an oxalate degrading enzyme for the treatment of hyperoxalurias; and an enzyme that degrades phenylalanine for the treatment of phenylketonuria. 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-237

Our lead preclinical product candidate, ALTU-237, is an orally-administered crystalline formulation of an oxalate-degrading enzyme which we have designed for the treatment of primary hyperoxaluria and enteric hyperoxaluria, as well as to prevent the recurrence of kidney stones in individuals with a risk or history of recurrent kidney stones. There are no current effective pharmacological treatments for primary hyperoxaluria, enteric hyperoxaluria or recurrent kidney stones. We plan to file an IND for ALTU-237 for the treatment of hyperoxalurias in early 2007.

Primary hyperoxaluria is a rare, inherited and, if left untreated, fatal metabolic disease that results in the accumulation of oxalate in the body. Oxalate is the salt form of oxalic acid, and is a natural end product of metabolism. Oxalate does not appear to be needed for any human body process, and in healthy individuals more than 90% of oxalate is excreted by the kidney, with a small amount of excretion into the lower gut. 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. Enteric hyperoxaluria is a condition resulting from increased intestinal absorption of oxalate, resulting in recurrent kidney and urinary stones. Enteric hyperoxaluria can occur in people who have intestinal diseases, such as Crohn s Disease and inflammatory bowel disease or may occur in patients following gastric surgery.

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 an estimated 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.

In our preclinical studies using rodent models, ALTU-237, delivered orally, demonstrated an ability to reduce oxalate levels in urine. We believe that these results suggest that we may be able to use our proprietary protein crystallization technology to orally deliver enzymes to the gastrointestinal tract, where they can exert a therapeutic effect by drawing out toxic metabolites from the body. This therapeutic approach is currently utilized by some existing drugs. For example, Renagel, marketed by Genzyme Corporation, removes excess levels of phosphate in the body in patients with chronic kidney disease by delivering drug to the gastrointestinal tract, where it binds to the phosphate and removes it from the body. If we are successful in our design of ALTU-237, we believe that this program will provide a template for our other research and preclinical programs that rely on the same fundamental science and mechanism of action.

ALTU-236

We are also developing ALTU-236, an orally-administered enzyme replacement therapy 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

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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 which 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. PKU and hyperphenylalanemia are currently treated by placing patients on a phenylalanine restricted diet. This diet is expensive and difficult to maintain and does not avoid many of the long-term effects of PKU. There are currently no approved drugs to treat PKU. We are currently testing ALTU-236 in animal models.

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 contrast, we are using our technology to crystallize proteins 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 ALTU-135, 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.

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 CFTTI have agreed to collaborate for the development of ALTU-135 and specified derivatives of ALTU-135 in North America for

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the treatment of malabsorption due to exocrine pancreatic insufficiency in patients with cystic fibrosis and other indications. The agreement, in general terms, provides us with funding from CFFTI for a portion of the development costs of ALTU-135 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 ALTU-135 to market in North America for the treatment of malabsorption due to exocrine pancreatic insufficiency in patients with cystic fibrosis and other indications. CFFTI has 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 ALTU-135. 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. We believe that our relationship with the Cystic Fibrosis Foundation will help facilitate our development of ALTU-135.

As of December 31, 2005, we had received a total of $18.4 million of the $25.0 million available under the agreement. In addition, we may receive an additional milestone payment of $6.6 million, less an amount determined by when we achieve the milestone. The alliance is managed by a steering committee, comprised of an equal number of representatives from Altus and CFFTI, which generally oversees the progress of our clinical development of ALTU-135 and reviews the schedule and achievement of milestones under our agreement.

Under the terms of the agreement, we granted CFFTI an exclusive license under our intellectual property rights covering ALTU-135 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. Our exclusive license to CFFTI continues in effect until the earliest to occur of our payment in full of all license fees due under the agreement, as described below; our termination of the agreement on account of a material default or bankruptcy of CFFTI; the parties mutual agreement not to proceed with development following a deadlock of the alliance steering committee; or the alliance steering committee s determination that ALTU-135 is not safe or effective for the treatment of exocrine pancreatic insufficiency or, solely due to scientific or medical reasons, that ALTU-135 should not be developed or marketed.

Our exclusive sublicense from CFFTI continues in effect until our license to CFFTI terminates or CFFTI terminates the agreement on account of our failure to meet specified milestones, our determination not to continue development after an unresolved deadlock of the alliance steering committee, or our material default or bankruptcy. If CFFTI terminates the agreement due to our breach, it would retain its exclusive license to ALTU-135 and our sublicense from CFFTI would terminate. Upon termination of the agreement by us due to a breach by CFFTI, the license granted to CFFTI to ALTU-135 will terminate.

If ALTU-135 is approved by the FDA, we are obligated to pay CFFTI a license fee equal to the aggregate amount of milestone payments we have received from CFFTI, plus interest, up to a maximum of $40.0 million, less the fair market value at the time of approval of the shares of stock underlying the warrants we issued to CFFTI. This fee, together with accrued interest, will be due in four annual installments, commencing 30 days after the approval date. We are required to pay an additional $1.5 million to CFFTI within 30 days after the approval date. In addition, we are obligated to pay royalties to CFFTI on worldwide net sales by us or our sublicensees of ALTU-135 for any and all indications until the expiration of specified United States patents covering ALTU-135. We have the option to terminate our ongoing royalty obligation by making a one-time payment to CFFTI but we currently do not expect to do so. We are also required to pursue, prosecute, maintain and defend all patents covered by the agreement at our own expense.

Dr. Falk Pharma GmbH

In December 2002, we entered into a development, commercialization and marketing agreement with Dr. Falk for the development by us of ALTU-135 and the commercialization by Dr. Falk of ALTU-135, if approved, in Europe, the countries of the former Soviet Union, Israel and Egypt. Under the agreement, we

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granted Dr. Falk an exclusive, sublicensable license under specified patents that cover ALTU-135 to commercialize ALTU-135 for the treatment of symptoms caused by exocrine pancreatic insufficiency.

As of December 31, 2005, we had received upfront and milestone payments from Dr. Falk under the agreement totaling 11.0 million. In addition, we may receive from Dr. Falk an additional 15.0 million in milestone payments based on the achievement of specified clinical and regulatory milestones. We are also eligible to receive royalties on net sales of ALTU-135 by Dr. Falk and its affiliates during the term of the license, as described below.

Under the terms of the agreement, each party is responsible for using commercially reasonable efforts to perform specified responsibilities relating to the development of ALTU-135, and Dr. Falk is responsible for using commercially reasonable efforts to obtain regulatory approvals and to commercialize ALTU-135 in the licensed territory. The agreement contemplates that, under the direction of a steering committee consisting of an equal number of representatives from Altus and Dr. Falk, we will conduct specified clinical trials, including an international Phase III clinical trial, required to support applications for regulatory approvals of ALTU-135 in the licensed territory. Dr. Falk has agreed to pay a portion of the development expenses, including costs relating to the process of obtaining regulatory approval, project management costs, statistical design and studies, and preparation of reports, that we incur in connection with the conduct of an international Phase III clinical trial. Expenses relating to other clinical trials conducted for the purpose of obtaining regulatory approvals in the licensed territory will be borne entirely by Dr. Falk.

The collaboration is coordinated through the steering committee. We maintain ultimate decision-making authority with respect to clinical development matters, subject to an obligation to exercise our decision-making authority in a manner that is consistent with the objective of managing an effective and efficient international Phase III clinical trial that satisfies the development, regulatory and commercialization requirements of the North American territory and the licensed territory and leveraging clinical development activities in both territories. Dr. Falk has responsibility for and control of commercialization matters in the licensed territory.

Under the agreement, we are responsible for supplying such quantities of ALTU-135 as may be required for the conduct of clinical trials, subject to the development expense allocation provisions of the agreement. We are also responsible for establishing a commercial scale manufacturing process for ALTU-135, for sourcing ALTU-135 from contract manufacturers, for ensuring that a second source supplier exists and, if Dr. Falk elects to purchase its requirements for commercial supply from us, for supplying Dr. Falk s requirements of ALTU-135 for commercial sale in the licensed territory. If Dr. Falk elects to purchase its requirements of ALTU-135 from us, which we expect it to do because we have not granted Dr. Falk a license to manufacture ALTU-135, the price at which Dr. Falk will purchase its requirements will equal the greater of a fixed percentage of specified Dr. Falk resale prices and our fully burdened manufacturing costs, and the other terms and conditions of supply will be governed by a commercial supply and distribution agreement to be negotiated by the parties. If our fully burdened manufacturing costs exceed the fixed percentage of the specified Dr. Falk resale prices, Dr. Falk is entitled to offset the excess against royalties due us up to a specified maximum offset amount.

Under the terms of the agreement, the license to Dr. Falk will continue in each country in the licensed territory until the later of the expiration of the last-to-expire of specified patents that cover ALTU-135 in that country or 12 years from the date of first commercial sale of ALTU-135 in that country. The current patents and the pending patent applications, if issued as patents, relating to ALTU-135 that are relevant to our agreement with Dr. Falk will expire between 2011 and 2025, excluding any extensions that we may receive. The agreement may be terminated by Dr. Falk for convenience by providing written notice to us within 30 days after Dr. Falk s receipt of the final report for the Phase III clinical trial of ALTU-135. In addition, subject to specified conditions, Dr. Falk may terminate the agreement if the manufacture, use or sale of ALTU-135 in the licensed territory is enjoined due to infringement of third-party patent rights or if a clinical hold with respect to ALTU-135 is imposed in a specified country. Either party may terminate the agreement upon the commitment of an uncured material breach by the other party or upon the

occurrence of specified bankruptcy or insolvency events involving the other party. Upon termination of the agreement by Dr. Falk due to a material breach by us, Dr. Falk will retain the license to ALTU-135 at a reduced royalty and have no further

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obligation to pay additional milestone payments. Upon termination of the agreement by us due to a material breach by Dr. Falk, the license granted to Dr. Falk to ALTU-135 will terminate.

Manufacturing

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of ALTU-135, ALTU-238 or any of the compounds that we are testing in our preclinical research and development programs. 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-135

Amano is currently our sole contract manufacturer of the crystallized and cross-linked lipase, the crystallized protease, and the amylase enzymes that comprise the active pharmaceutical ingredients, or APIs, for ALTU-135. We entered into a five-year cooperative development agreement with Amano in November 2002, which was amended in October 2005, to collaborate on process development and scale-up of API production for ALTU-135. Amano has built a plant in Nagoya, Japan to produce the enzymes for ALTU-135 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. Under our agreement, Amano has supplied the APIs for ALTU-135 for our non-clinical and clinical trials to date and has agreed to supply us with APIs for our Phase III clinical trial and additional toxicology studies at a specified transfer price. Under our agreement, Amano may not sell to other parties the APIs for ALTU-135 for use in specified competitive products. We use a third party to perform fill, finish and packaging services for ALTU-135.

Under the terms of the agreement, each party has contributed technology used for the production of the APIs in ALTU-135. Each party owns intellectual property created solely by it, and jointly owns any intellectual property created jointly. Pursuant to our agreement with Amano, they have notified us that they will not be the primary manufacturer of the APIs for the initial commercial supply of ALTU-135. We expect to negotiate a new agreement with Amano that governs the commercial supply of some of the APIs for ALTU-135. Amano will be required to grant licenses of its technology to other contract manufacturers which we mutually select, and we will be required to pay Amano a royalty based on the cost of the materials supplied to us by such other contract manufacturers. We are in the process of selecting a contract manufacturer that is capable of providing us commercial quantities of APIs for ALTU-135. We are obligated under our agreement with Amano to use best efforts to develop and commercialize ALTU-135.

Our agreement with Amano expires in November 2007, unless mutually extended by the parties. The agreement may be terminated by either party upon an uncured material breach by the other party or upon specified bankruptcy or insolvency events involving the other party. In addition, either party may terminate the agreement without cause on one year s written notice to the other party. If the agreement terminates for any reason, our licenses under the agreement survive forever and, in the case of a termination for our material breach or a termination by us for reasons other than Amano s material breach, we must pay Amano royalties on worldwide sales of ALTU-135.

ALTU-238

We currently purchase hGH from from Sandoz GmbH, or Sandoz, a subsidiary of Novartis AG, and we have no long-term supply arrangements or contracts. A product containing the hGH supplied by Sandoz has not been approved by the FDA but recently received a positive opinion from the EMEA s Committee on Medicinal Products for Human Use and was approved by the Australian Therapeutic Goods Administration. We are negotiating with various

manufacturers with respect to commercial supply agreements for hGH.

We completed small-scale cGMP runs of ALTU-238 at a contract manufacturer for our Phase I and II clinical trials. We expect that we will have to secure additional manufacturing capacity with one or more

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contract manufacturers in order to produce ALTU-238 for our subsequent trials and on a commercial scale. We also expect to arrange for a third party to perform fill, finish and packaging services for ALTU-238.

Sales and Marketing

If we receive regulatory approval for any of our product candidates, we plan to commence commercialization activities by building a focused sales and marketing organization. Our sales and marketing strategy is to:

Build our own North American sales force. We plan to establish a commercial infrastructure and targeted specialty sales force to market our product candidates in North America. Our sales efforts for ALTU-135, if approved, will initially be focused on the 500 pediatric pulmonologists who are in approximately 100 cystic fibrosis care centers throughout the United States, as well as the 5,000 key gastroenterologists and pancreatologists who prescribe products for exocrine pancreatic insufficiency. For ALTU-238, we plan to focus initially on the approximately 400 key prescribing pediatric endocrinologists and approximately 3,000 adult endocrinologists who treat patients with growth hormone deficiency. Because the target groups for ALTU-238 are primarily hospital-based and concentrated in major metropolitan areas, we believe that we can effectively address the market for ALTU-238 with a specialized sales force that targets these key prescribers. We also plan to leverage our sales and marketing capabilities by targeting the same groups of physician specialists with multiple products that we bring to market either through our own development efforts or by in- licensing from others.

Assemble a marketing organization. We plan to build a marketing, managed care and sales management organization to create and implement marketing strategies for ALTU-135, ALTU-238 and other product candidates in our product pipeline. We expect that our marketing organization will oversee any products that we market through our own sales force and oversee and support our sales and reimbursement efforts. The responsibilities of the marketing organization will include developing educational initiatives with respect to approved products and establishing relationships with thought leaders in relevant fields of medicine. We also plan to conduct post-approval marketing studies for our products to provide further data on the safety and efficacy. As we develop our pipeline products, we will evaluate whether to expand our marketing and sales efforts.

Selectively establish collaborations for our product candidates with leading pharmaceutical and biotechnology companies. We may enter into additional collaborations in markets outside of North America where we believe that having a partner will enable us to gain better access to those markets. In addition, we may co-commercialize our product candidates in North America with pharmaceutical and biotechnology companies to achieve a variety of business objectives including expanding the market or accelerating penetration. We may also collaborate with such companies to accelerate the development of selected early-stage product candidates.

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 may 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 recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or

necessary for, 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

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

ALTU-135. If approved, ALTU-135, the product candidate we are developing for the treatment of malabsorption due to exocrine pancreatic insufficiency, will compete with currently marketed porcine-derived pancreatic enzyme replacement therapies from Axcan Pharma, Johnson & Johnson, and Solvay Pharmaceuticals, as well as from generic drug manufacturers such as KV Pharmaceutical and IMPAX Laboratories. In April 2004, the FDA issued a notice that manufacturers of existing pancreatic enzyme replacement products will be subject to regulatory action if they do not obtain approved NDAs for these products by April 28, 2008. We believe that some of the manufacturers of these products may not be able to satisfy the FDA s requirements for NDAs. In addition, we understand that Biovitrum, Eurand and Meristem Therapeutics have product candidates in clinical development that could compete with ALTU-135. However, the product candidates from Biovitrum and Meristem contain only lipase and we believe that the product candidate from Eurand is porcine-derived.

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 Genentech, Pfizer, Serono, Novo Nordisk, Teva Pharmaceutical Industries and Eli Lilly. 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.

Key differentiating elements affecting the success of all 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 not 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 that are not yet in clinical trials.

As of December 31, 2005, our patent estate on a worldwide basis includes 12 patents issued in the United States, 20 issued in current member states of the European Patent Convention and 19 issued in other counties, 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.

Four of our issued United States patents, expiring between 2014 and 2016, relate to ALTU-135 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 four pending United States patent applications relating to ALTU-135, which if issued as patents, would expire between 2017 and 2025. Some of these applications

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include claims covering a combination of lipase, protease and amylase in specific formulations and methods of treatment using these formulations. We also have 29 issued foreign patents, expiring between 2011 and 2021, relating to ALTU-135 and pending foreign patent applications, which if issued as patents, would expire between 2011 and 2025.

We have three pending United States patent applications relating to ALTU-238, which if issued as patents, would expire between 2023 and 2026, 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 30 pending foreign patent applications relating to ALTU-238, which if issued as patents, would expire in 2023.

Our patent estate includes patent applications relating to some of our other product candidates. Some of these applications are pending in the United States and foreign patent offices. Others have to date only been filed in the United States. We expect to file these outside of the United States at the appropriate time. These patent applications, assuming they issue as patents, would expire between 2017 and 2026. 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, specific methods of making cross-linked crystals with controlled dissolution properties, 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 ALTU-135 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.

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

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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;

a clinical hold;

warning letters;

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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 IND, which must become effective before human clinical trials may begin;

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

submission to the FDA of a 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. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP. These regulations include the requirement that all research subjects provide informed consent. Further, an 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.

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.

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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 a clinical trial at any time on various grounds, 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, packed 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 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.

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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.

Continuous Marketing Applications Pilot 2

In conjunction with the reauthorization of the Prescription Drug User Fee Act of 1992, or PDUFA, the FDA agreed to meet specific performance goals, one of which was to conduct pilot programs to explore CMAs. Under one of the CMA pilot programs called Pilot 2, one fast-track designated product from each review division of CDER and CBER is selected for frequent scientific feedback and interactions with the FDA, with a goal of improving the efficiency and effectiveness of the drug development process. In order to be eligible for participation, the drug or biologic must (1) have been designated fast track, (2) have been the subject of an end-of-Phase I meeting or another type of meeting that FDA determines is equivalent, and (3) not be on clinical hold. Applicants must make a formal application as described in an FDA Guidance on the subject and will be evaluated based on the FDA s overall assessment of:

the potential value of enhanced interaction, emphasizing the potential public health benefit resulting from development of the product;

the likelihood that concentrated scientific dialogue will facilitate the availability of a promising novel therapy; and

the applicant s demonstration of commitment to product development as evidenced by a thorough consideration of the rationale for participation in Pilot 2.

A maximum of one fast-track product per review division in CDER and CBER will be chosen to participate.

Once an applicant is selected for participation in Pilot 2, the review division and the applicant will finalize an agreement on the nature of the timelines for feedback and interactions between the applicant and the FDA. Pilot 2 agreements and activities for each application will continue through September 30, 2007, the pilot program completion date, unless (1) an NDA or BLA is submitted, (2) the applicant withdraws the product from the pilot program, or (3) the agreement is terminated by the FDA because the drug or biologic no longer meets the pre-application criteria or the applicant deviates significantly from the negotiated developmental plan or has other significant disagreements with FDA.

In November 2003, ALTU-135 was granted a fast track designation for treatment of malabsorption in patients with partial or complete exocrine pancreatic insufficiency. In February 2004, ALTU-135 was accepted into the Pilot 2

program pending agreement on a schedule of interactions with the FDA.

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Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor s product for the same indication or dise