HALOZYME THERAPEUTICS INC
Form 424B5
September 08, 2010

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Filed Pursuant to Rule 424(b)(5)
Registration Nos. 333-164215

This preliminary prospectus supplement relates to an effective registration statement under the Securities Act of 1933, but is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion, dated September 8, 2010

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated January 5, 2010)

8,300,000 Shares

Common Stock

This is an offering of 8,300,000 shares of the common stock of Halozyme Therapeutics, Inc.

Our common stock is listed on The NASDAQ Global Market under the symbol HALO. The last reported sale price of our common stock on The NASDAQ Global Market on September 3, 2010 was $7.99 per share.

Investing in our common stock involves significant risks. See Risk Factors beginning on page S-7 of this prospectus supplement and each of the Risk Factors on page 4 of the accompanying prospectus.

	Per Share	Total
Price to the public	$	$
Underwriting discounts and commissions	$	$
Proceeds to Halozyme Therapeutics, Inc. (before expenses)	$	$

We have granted Barclays Capital a 30-day option to purchase up to an additional 1,245,000 shares of common stock on the same terms and conditions set forth above.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus supplement or the prospectus to which it relates. Any representation to the contrary is a criminal offense.

Barclays Capital expects to deliver the shares on or about September , 2010.

Barclays Capital

Prospectus Supplement dated September , 2010

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No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement or the accompanying prospectus. You must not rely on any unauthorized information or representations. This prospectus supplement and the accompanying prospectus are an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of their respective dates.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated January 5, 2010, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectus that we have authorized for use in connection with this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. We have not authorized anyone to provide you with different or additional information. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the respective dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus, and may not contain all of the information that is important to you. This prospectus supplement and the accompanying prospectus include information about the offering as well as information regarding our business. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety. If you invest in our common stock, you are assuming a high degree of risk. See Risk Factors beginning on page S-7.

Our Business

Overview

We are a biopharmaceutical company dedicated to the development and commercialization of products targeting the extracellular matrix for the endocrinology, oncology, dermatology and drug delivery markets. Our existing products and our products under development are based primarily on intellectual property covering the family of human enzymes known as hyaluronidases. Hyaluronidases are enzymes (proteins) that break down hyaluronan, or HA, which is a naturally occurring space-filling, gel-like substance that is a major component of both normal tissues throughout the body, such as skin and cartilage, and abnormal tissues such as tumors. Our primary technology is based on our proprietary recombinant human PH20 enzyme, or rHuPH20, a human synthetic version of hyaluronidase. The PH20 enzyme is a naturally occurring enzyme that temporarily degrades HA, thereby facilitating the penetration and diffusion of other drugs and fluids that are injected under the skin or in the muscle. Our proprietary rHuPH20 technology is applicable to multiple therapeutic areas and may be used to both expand existing markets and create new ones through the development of our own proprietary products. The rHuPH20 technology may also be applied to existing and developmental products of third parties through key partnerships.

Our operations to date have involved organizing and staffing our operating subsidiary, Halozyme, Inc., acquiring, developing and securing our technology and undertaking product development for our existing products and a limited number of product candidates. We continue to increase our focus on our proprietary product pipeline and have expanded investments in our proprietary product candidates. We currently have multiple proprietary programs in various stages of research and development. In addition, we have entered into a key partnership with F. Hoffmann-La Roche, Ltd and Hoffmann-La Roche, Inc., or Roche, to apply our Enhanze™ Technology to Roche s biological therapeutic compounds for up to 13 targets. We have also entered into two key partnerships with Baxter Healthcare Corporation, or Baxter, to apply Enhanze Technology to Baxter s biological therapeutic compound, GAMMAGARD LIQUID™ and to develop and supply active pharmaceutical ingredient, or API, for HYLENEX®. There are two marketed products that utilize our technology: HYLENEX, a product used as an adjuvant to enhance the dispersion and absorption of other injected drugs and fluids, and Cumulase®, a product used for *in vitro* fertilization, or IVF.

Because a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying HYLENEX agreements, HYLENEX was voluntarily recalled in May 2010. On May 16, 2010, we delivered a notice of breach to Baxter due to Baxter s failure to manufacture HYLENEX in accordance with the terms of existing development and supply contracts. The notice of breach was sent after Baxter informed us that a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying agreements with Baxter. In July of 2010, Baxter asserted their own breach claims against us, which we believe are without merit, and we expect to prevail in the event of any dispute relating to the HYLENEX agreements. On August 31, 2010, we

announced the completion of our root cause investigation regarding HYLENEX manufacturing and also withdrawal of the notice of breach. We have identified a corrective action plan and regulatory strategy to reintroduce HYLENEX to the market. We hope to meet with the U.S. Food and Drug Administration

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(FDA) in the near future and we will not be able to predict the timing for HYLENEX reintroduction until after meeting with the FDA. Currently, we receive only limited revenue from the sales of API for HYLENEX and the sales of API to the third party that produces Cumulase, in addition to other revenues from our partnerships with Baxter and Roche.

We have product candidates in the research, preclinical and clinical stages, but future revenues from the sales of these product candidates will depend on our ability to develop, manufacture, obtain regulatory approvals for and successfully commercialize product candidates. It may be years, if ever, before we are able to obtain regulatory approvals for these product candidates. We have incurred net operating losses each year since inception, with an accumulated deficit of approximately $195.9 million as of June 30, 2010.

Products and Product Candidates

We have two marketed products and multiple product candidates targeting several indications in various stages of development. The following table summarizes our proprietary products and product candidates as well as our partnered products and product candidates:

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Ultrafast Insulin Program

Our lead proprietary program focuses on the formulation of rHuPH20 with prandial (mealtime) insulins for the treatment of diabetes mellitus. Diabetes mellitus is an increasingly prevalent, costly condition associated with substantial morbidity and mortality. Attaining and maintaining normal blood sugar levels to minimize the long-term clinical risks is a key treatment goal for diabetic patients. Combining rHuPH20 with regular insulin (such combinations are referred to as Insulin-PH20) or a rapid acting analog insulin, i.e., insulin lispro (Humalog®), insulin aspart (Novolog®) and insulin glulisine (Apidra®) (such combinations are referred to as Analog-PH20), facilitates faster insulin dispersion in, and absorption from, the subcutaneous space into the vascular compartment leading to faster insulin response. By making mealtime insulin onset faster, i.e., providing earlier insulin to the blood and thus earlier glucose lowering activity, a combination of insulin with rHuPH20 may yield a better profile of insulin effect, more like that found in healthy, non-diabetic people.

The primary goal of our ultrafast insulin program is to develop a best-in-class insulin product, with demonstrated clinical benefits for type 1 and 2 diabetes mellitus patients, in comparison to the current standard of care analog products that participate in the growing $3.8 billion prandial insulin market. We are developing Insulin-PH20 and Analog-PH20 in parallel to explore a maximum range of value creating opportunities. With a more rapidly absorbed, faster acting insulin product, we seek to demonstrate one or more significant improvements relative to existing treatment, such as improved glycemic control, less hypoglycemia, and less weight gain. A number of Phase 1 and Phase 2 clinical pharmacology trials, and registration trial-enabling treatment studies in connection with our ultrafast insulin program are ongoing or planned, that will investigate the various attributes of our insulin product candidates.

On September 2, 2010, we announced the initiation of two randomized double-blind Phase 2 clinical trials, one in patients with type 1 diabetes and the other in patients with type 2 diabetes, each designed to compare two investigational drug products, Aspart-PH20 and Lispro-PH20, for medical benefits such as improved glycemic control (A1C), reduced hypoglycemia, and/or reduced weight gain relative to a standard of care therapy. Each study has a primary objective of demonstrating non-inferiority in A1C, although they also have sufficient power to demonstrate a meaningful improvement in A1C for either investigational drug relative to the active comparator in either patient population.

PEGPH20

We are investigating a PEGylated version of rHuPH20, or PEGPH20, a new molecular entity, as a candidate for the systemic treatment of tumors rich in HA. PEGylation refers to the attachment of polyethylene glycol to our rHuPH20 enzyme, which extends its half life in the blood from less than one minute to approximately 48-72 hours. An estimated 20% to 30% of solid tumors, including prostate, breast, pancreas and colon, accumulate significant amounts of HA that forms a halo-like coating over the surface of the tumor. The quantity of HA produced by the tumor correlates with increased tumor growth and metastasis and has been linked with tumor progression in some studies.

In the first quarter of 2009, we initiated a Phase 1 clinical trial for our PEGPH20 program. This first in human trial with PEGPH20 is a dose-escalation, multicenter, pharmacokinetic and pharmacodynamic, safety study, in which patients with advanced solid tumors are receiving intravenous administration of PEGPH20 as a single agent. Based on initial data from this trial, and after consultation with the FDA, lower doses of PEGPH20 are now employed at a lower dosing frequency. The study is actively enrolling and in a dose escalation phase. In July 2010, we initiated a second Phase 1 clinical trial with PEGPH20 in the treatment of solid tumors. The new trial incorporates the use of oral dexamethasone as a pretreatment for all patients prior to receiving intravenous administration of PEGPH20.

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Enhanze Technology

Enhanze Technology, a proprietary drug delivery enhancement platform using rHuPH20, is a broad technology that we have licensed to other pharmaceutical companies. When formulated with other injectable drugs, Enhanze Technology can facilitate the subcutaneous dispersion and absorption of these drugs. Molecules as large as 200 nanometers may pass freely through the extracellular matrix, which recovers its normal density within approximately 24 hours, leading to a drug delivery platform which does not permanently alter the architecture of the skin. The principal focus of our Enhanze Technology platform is the use of rHuPH20 to facilitate subcutaneous route of administration for large molecule biological therapeutics, some of which currently require intravenous administration. Potential benefits of subcutaneous administration of these biologics include life cycle management, patient convenience, reductions in infusion reactions and benefits to payors.

We currently have Enhanze Technology partnerships with Roche and Baxter and we are currently pursuing additional partnerships with biopharmaceutical companies that market or develop drugs that could benefit from injection via the subcutaneous route of administration.

Roche Partnership

In December 2006, Halozyme and Roche entered into an Enhanze Technology partnership, or the Roche Partnership. Under the terms of the Roche Partnership, Roche obtained a worldwide, exclusive license to develop and commercialize product combinations of rHuPH20 with up to thirteen Roche target compounds resulting from the collaboration. Roche initially had the exclusive right to apply rHuPH20 to only three pre-defined Roche biologic targets with the option to exclusively develop and commercialize rHuPH20 with an additional ten targets. Roche elected to add a fourth exclusive target to the three original exclusive targets in December 2008 and a fifth exclusive target in June 2009. Roche retains the option to exclusively develop and commercialize rHuPH20 with an additional eight targets through the payment of annual license maintenance fees. Pending the successful completion of various clinical, regulatory and sales events, Roche will be obligated to make milestone payments to us, as well as royalty payments on the sales of products that result from the partnership.

Compounds directed at three of the Roche exclusive targets have previously commenced clinical trials. One compound is in a Phase 1 clinical trial, one compound has completed a Phase 1 clinical trial and the third compound is in a Phase 3 clinical trial. In October 2009, Roche commenced the first Phase 3 clinical trial for a compound directed at an exclusive target. This Phase 3 clinical trial is for a subcutaneously delivered version of Roche s anticancer biologic, Herceptin (trastuzumab). The study will investigate the pharmacokinetics, efficacy and safety of subcutaneous Herceptin in patients with HER2-positive breast cancer as part of adjuvant treatment. Herceptin is approved to treat HER2-positive breast cancer and currently is given intravenously. Breast cancer is the most common cancer among women worldwide. Each year, more than one million new cases of breast cancer are diagnosed worldwide, and nearly 400,000 people will die of the disease annually. In HER2-positive breast cancer, increased quantities of the HER2 protein are present on the surface of the tumor cells. This is known as HER2 positivity and affects approximately 20-25% of women with breast cancer.

In September 2009, Roche began a Phase 1 clinical trial for a subcutaneous formulation of MabThera® (rituximab). The study will investigate the pharmacokinetics and tolerability of subcutaneous MabThera in patients with follicular lymphoma as part of maintenance treatment. Intravenously administered MabThera is approved for the treatment of non-Hodgkin s lymphoma (NHL), a type of cancer that affects lymphocytes, or white blood cells. An estimated 66,000 new cases of NHL were diagnosed in the U.S. in 2009 with approximately 125,000 new cases reported worldwide.

Additional information about the Phase 3 subcutaneous Herceptin and Phase 1 subcutaneous MabThera clinical trials can be found at www.clinicaltrials.gov and www.roche-trials.com.

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Baxter Gammagard Partnership

GAMMAGARD LIQUID is a current Baxter product that is indicated for the treatment of primary immunodeficiency disorders associated with defects in the immune system. In September 2007, Halozyme and Baxter entered into an Enhanze Technology partnership, or the Gammagard Partnership. Under the terms of this partnership, Baxter obtained a worldwide, exclusive license to develop and commercialize product combinations of rHuPH20 with GAMMAGARD LIQUID. Pending the successful completion of various regulatory and sales milestones, Baxter will be obligated to make milestone payments to us, as well as royalty payments on the sales of products that result from the partnership. Baxter is responsible for all development, manufacturing, clinical, regulatory, sales and marketing costs under the Gammagard Partnership, while we will be responsible for the supply of the rHuPH20 enzyme. In addition, Baxter has certain product development and commercialization obligations in major markets identified in the Gammagard License. In January of 2009, Baxter commenced a Phase 3 clinical trial for GAMMAGARD LIQUID with rHuPH20, and in July 2009, the enrollment for this study was completed.

HYLENEX Partnership

HYLENEX is a formulation of rHuPH20 that, when injected under the skin, enhances the dispersion and absorption of other injected drugs or fluids. In February 2007, Halozyme and Baxter amended certain existing agreements relating to HYLENEX and entered into a new agreement for kits and formulations with rHuPH20, or the HYLENEX Partnership. Pending the successful completion of a series of regulatory and sales events, Baxter will be obligated to make milestone payments to us, as well as royalty payments on the sales of products that result from the partnership. Baxter is responsible for development, manufacturing, clinical, regulatory, sales and marketing costs of the products covered by the HYLENEX Partnership. We will continue to supply Baxter with API for HYLENEX, and Baxter will prepare, fill, finish and package HYLENEX and hold it for subsequent distribution.

Because a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying HYLENEX agreements, HYLENEX was voluntarily recalled in May 2010. On May 16, 2010, we delivered a notice of breach to Baxter due to Baxter s failure to manufacture HYLENEX in accordance with the terms of existing development and supply contracts. The notice of breach was sent after Baxter informed us that a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying agreements with Baxter. In July of 2010, Baxter asserted their own breach claims against us, which we believe are without merit, and we expect to prevail in the event of any dispute relating to the HYLENEX agreements. On August 31, 2010, we announced the completion of our root cause investigation regarding HYLENEX manufacturing and also withdrawal of the notice of breach. We have identified a corrective action plan and regulatory strategy to reintroduce HYLENEX to the market. We hope to meet with the FDA in the near future and we will not be able to predict the timing for HYLENEX reintroduction until after meeting with the FDA.

Corporate Information

We reincorporated from the State of Nevada to the State of Delaware in November 2007. Our principal offices and research facilities are located at 11388 Sorrento Valley Road, San Diego, California 92121. Our telephone number is (858) 794-8889 and our e-mail address is info@halozyme.com. Additional information about us can be found on our website at www.halozyme.com. The information on our website is not part of this prospectus supplement.

Unless the context indicates otherwise or we expressly state to the contrary, as used in this prospectus supplement and the accompanying prospectus, the terms the Company, Halozyme, Halozyme Therapeutics, we, us and our re Halozyme Therapeutics, Inc., a Delaware corporation, and our operating subsidiary, Halozyme, Inc.

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THE OFFERING

Common stock we are offering	8,300,000 shares
Common stock covered by the underwriter s option to purchase additional shares	1,245,000 shares
Common stock outstanding immediately following this offering (excluding any shares subject to the underwriter s option to purchase additional shares)	100,324,742 shares
Risk Factors	Investing in our common stock involves a high degree of risk. See Risk factors beginning on page S-7.
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes and to support further research and development of our product candidates. See Use of Proceeds on page S-20.
NASDAQ Global Market symbol	HALO

The number of shares of common stock to be outstanding immediately after this offering as shown above assumes that all of the shares offered hereby are sold and is based on 92,024,742 shares of common stock outstanding as of August 2, 2010. This number of shares does not include 1,245,000 shares subject to the underwriter s option to purchase additional shares and also excludes, as of August 2, 2010:

- 8,610,097 shares of common stock issuable upon the exercise of outstanding stock options, having a weighted average exercise price of $3.98 per share; and
- an aggregate of up to 2,877,934 shares of common stock reserved for future issuance under our stock option and employee stock purchase plans.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business.

Risks Relating to this Offering and Ownership of Our Common Stock

Our stock price is subject to significant volatility.

We participate in a highly dynamic industry which often results in significant volatility in the market price of common stock irrespective of company performance. As a result, our high and low sales prices of our common stock during the twelve months ended June 30, 2010 were $9.11 and $5.22, respectively. We expect our stock price to continue to be subject to significant volatility and, in addition to the other risks and uncertainties described elsewhere in this prospectus supplement and all other risks and uncertainties that are either not known to us at this time or which we deem to be immaterial, any of the following factors may lead to a significant drop in our stock price:

- a dispute regarding our failure, or the failure of one of our third party partners, to comply with the terms of a collaboration agreement;
- the termination, for any reason, of any of our collaboration agreements;
- the sale of common stock by any significant stockholder, including, but not limited to, direct or indirect sales by members of management or our Board of Directors;
- the resignation, or other departure, of members of management or our Board of Directors;
- general negative conditions in the healthcare industry;
- general negative conditions in the financial markets;
- the failure, for any reason, to obtain regulatory approval for any of our proprietary or partnered product candidates;
- the failure, for any reason, to secure or defend our intellectual property position;
- for those products that are approved by the FDA, the failure of the FDA to approve such products in a timely manner consistent with the FDA s historical approval process;
- the suspension of any clinical trial due to safety or patient tolerability issues;
- the suspension of any clinical trial due to market and/or competitive conditions;

our failure, or the failure of our third party partners, to successfully commercialize products approved by applicable regulatory bodies such as the FDA;

our failure, or the failure of our third party partners, to generate product revenues anticipated by investors;

problems with an API contract manufacturer or a fill and finish manufacturer for any product or product candidate;

the sale of additional debt and/or equity securities by us;

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our failure to obtain financing on acceptable terms; or

a restructuring of our operations.

Future sales of shares of our common stock pursuant to our universal shelf registration statement may negatively affect our stock price.

Sales of a substantial number of shares of our common stock in the public market after this offering, or the perception that these sales might occur, could depress the market price of our common stock, and could impair our ability to raise capital through the sale of additional equity securities. As of June 30, 2010, we had 92,010,298 shares of common stock outstanding, all of which shares are eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale and other requirements under Rule 144, the restrictions under our NOL preservation lock-up agreement described under Description of Capital Stock in the accompanying prospectus and the restrictions under the lock-up agreements with Barclays Capital described under Underwriting in this prospectus supplement. In addition, all of the shares of common stock sold in this offering will be freely tradeable

Trading in our stock has historically been limited, so investors may not be able to sell as much stock as they want to at prevailing market prices.

Our stock has historically traded at a low daily trading volume. If low trading volume continues, it may be difficult for stockholders to sell their shares in the public market at any given time at prevailing prices.

If you purchase shares of common stock in this offering, you will experience immediate and substantial dilution in your investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions.

Purchasers of common stock in this offering will pay a price per share in this offering that substantially exceeds the net tangible book value (deficit) per share of our common stock. Assuming we sell 8,300,000 shares of our common stock in this offering at an assumed public offering price of $7.99 per share (which was the last reported sale price of our common stock as reported on The NASDAQ Global Market on September 3, 2010), without any deduction for underwriting discounts and commissions but after deducting estimated offering expenses payable by us, you would experience immediate and substantial dilution of $7.47 per share, representing the difference between our as adjusted net tangible book value (deficit) per share as of June 30, 2010 after giving effect to this offering and the assumed public offering price. See the section entitled Dilution below for a more detailed illustration of the dilution you would incur if you purchase common stock in this offering.

If we raise additional funds by issuing additional common stock, or securities convertible into or exchangeable or exercisable for common stock, our stockholders, including investors who purchase shares of common stock in this offering, will experience additional dilution, and any such issuances may result in downward pressure on the price of our common stock.

Risks Related To Our Business

We have generated only minimal revenue from product sales to date; we have a history of net losses and negative cash flow, and we may never achieve or maintain profitability.

Relative to expenses incurred in our operations, we have generated only minimal revenue from product sales, licensing fees and milestone payments to date and we may never generate sufficient revenues from future product

sales, licensing fees and milestone payments to offset expenses. Even if we ultimately do achieve significant revenues from product sales, licensing fees and/or milestone payments, we expect to incur significant operating losses over the next few years. We have never been

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profitable, and we may never become profitable. Through June 30, 2010, we have incurred aggregate net losses of approximately $195.9 million.

If our contract manufacturers are unable to manufacture significant amounts of the API used in our products and product candidates, our product development and commercialization efforts could be delayed or stopped and our collaborative partnerships could be damaged.

We have existing supply agreements with contract manufacturing organizations Avid Bioservices, Inc., or Avid, and Cook Pharmica LLC, or Cook, to produce bulk API. These manufacturers each produce API under current Good Manufacturing Practices, or cGMP, for clinical uses. In addition, Avid currently produces API for commercialized products. Avid and Cook will also provide support for the chemistry, manufacturing and controls sections for FDA and other regulatory filings. We rely on their ability to successfully manufacture these batches according to product specifications and Cook has relatively limited experience manufacturing our API. In addition, as a result of our contractual obligations to Roche, we will be required to significantly scale up our commercial API production at Cook during the next few years. If Cook is unable to obtain status as a cGMP-approved manufacturing facility, or if either Avid or Cook: (i) are unable to retain status as cGMP-approved manufacturing facilities; (ii) are unable to otherwise successfully scale up our API production; or (iii) fail to manufacture the API required by our proprietary and partnered products and product candidates for any other reason, our business will be adversely affected. We have not established, and may not be able to establish, favorable arrangements with additional API manufacturers and suppliers of the ingredients necessary to manufacture the API should the existing manufacturers and suppliers become unavailable or in the event that our existing manufacturers and suppliers are unable to adequately perform their responsibilities. We have attempted to mitigate the impact of supply interruption through the establishment of excess API inventory, but there can be no assurances that this safety stock will be maintained or that it will be sufficient to address any delays, interruptions or other problems experienced by Avid and/or Cook. Any delays, interruptions or other problems regarding the ability of Avid and/or Cook to supply API on a timely basis could: (i) cause the delay of clinical trials or otherwise delay or prevent the regulatory approval of proprietary or partnered product candidates; (ii) delay or prevent the effective commercialization of proprietary or partnered products and/or (iii) cause us to breach contractual obligations to deliver API to our partners. Such delays would likely damage our relationship with our partners under our key collaboration agreements and they would have a material adverse effect on our business and financial condition.

Our key partners are responsible for providing certain proprietary materials that are essential components of our partnered product candidates, and any failure to supply these materials could delay the development and commercialization efforts for these partnered product candidates and/or damage our collaborative partnerships.

Our partners are responsible for providing certain proprietary materials that are essential components of our partnered product candidates. For example, Roche is responsible for producing the Herceptin and MabThera required for its subcutaneous product candidates and Baxter is responsible for producing the GAMMAGARD LIQUID for its product candidate. If a partner, or any applicable third party service provider of a partner, encounters difficulties in the manufacture, storage, delivery, fill, finish or packaging of either components of the partnered product candidate or the partnered product candidate itself, such difficulties could: (i) cause the delay of clinical trials or otherwise delay or prevent the regulatory approval of partnered product candidates; and/or (ii) delay or prevent the effective commercialization of partnered products. Such delays could have a material adverse effect on our business and financial condition. For example, Baxter received a Warning Letter from the FDA in January 2010 regarding Baxter s GAMMAGARD LIQUID manufacturing facility in Lessines, Belgium. The FDA indicated in March 2010 that the issues raised in the Warning Letter had been addressed by Baxter and we do not expect these issues to impact the development of the GAMMAGARD LIQUID product candidate.

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If any party to a key collaboration agreement, including us, fails to perform material obligations under such agreement, or if a key collaboration agreement, or any other collaboration agreement, is terminated for any reason, our business could significantly suffer.

We have entered into multiple collaboration agreements under which we may receive significant future payments in the form of maintenance fees, milestone payments and royalties. In the event that a party fails to perform under a key collaboration agreement, or if a key collaboration agreement is terminated, the reduction in anticipated revenues could delay or suspend our product development activities for some of our product candidates, as well as our commercialization efforts for some or all of our products. In addition, the termination of a key collaboration agreement by one of our partners could materially impact our ability to enter into additional collaboration agreements with new partners on favorable terms, if at all. In certain circumstances, the termination of a key collaboration agreement would require us to revise our corporate strategy going forward and reevaluate the applications and value of our technology.

For example, because a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying HYLENEX agreements, HYLENEX was voluntarily recalled in May 2010. On May 16, 2010, we delivered a notice of breach to Baxter due to Baxter s failure to manufacture HYLENEX in accordance with the terms of existing development and supply contracts. The notice of breach was sent after Baxter informed us that a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying agreements with Baxter. In July of 2010, Baxter asserted their own breach claims against us, which we believe are without merit, and we expect to prevail in the event of any dispute relating to the HYLENEX agreements. On August 31, 2010, we announced the completion of our root cause investigation regarding HYLENEX manufacturing and also withdrawal of the notice of breach. We have identified a corrective action plan and regulatory strategy to reintroduce HYLENEX to the market. We hope to meet with the FDA in the near future and we will not be able to predict the timing for HYLENEX reintroduction until after meeting with the FDA.

If we have problems with third parties that either distribute API on our behalf or prepare, fill, finish and package our products and product candidates for distribution, our commercialization and development efforts for our products and product candidates could be delayed or stopped.

We rely on third parties to store and ship API on our behalf and to also prepare, fill, finish and package our products and product candidates prior to their distribution. If we are unable to locate third parties to perform these functions on terms that are acceptable to us, the progress of clinical trials could be delayed or even suspended and the commercialization of approved product candidates could be delayed or prevented. We currently utilize a subsidiary of Baxter to prepare, fill, finish and package HYLENEX under a development and supply agreement. We rely on its ability to successfully manufacture HYLENEX batches according to product specifications. Any delays or interruptions in Baxter s ability to manufacture HYLENEX batches in amounts necessary to meet product demand could have a material adverse impact on our business and financial condition.

For example, because a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying HYLENEX agreements, HYLENEX was voluntarily recalled in May 2010. On August 31, 2010, we announced the completion of our root cause investigation regarding HYLENEX manufacturing, and we have identified a corrective action plan and regulatory strategy to reintroduce HYLENEX to the market. We hope to meet with the FDA in the near future and we will not be able to predict the timing for HYLENEX reintroduction until after meeting with the FDA.

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We may wish to raise additional capital in the next twelve months, and there can be no assurance that we will be able to obtain such funds.

During the next twelve months, we may wish to raise additional capital to continue the development of our product candidates or for other current corporate purposes. Our current cash position and expected revenues during the next few years will not constitute the amount of capital necessary for us to continue the development of our proprietary product candidates and to fund general operations. In addition, if we engage in acquisitions of companies, products or technology in order to execute our business strategy, we may need to raise additional capital. We will need to raise additional capital in the future through one or more financing vehicles that may be available to us. Potential financing vehicles include: (i) the public or private issuance of securities; (ii) new collaborative agreements; and/or (iii) expansions or revisions to existing collaborative relationships.

Considering our stage of development, the nature of our capital structure and general market conditions, if we are required to raise additional capital in the future, the additional financing may not be available on favorable terms, or at all. If additional capital is not available on favorable terms, we will be required to significantly reduce operating expenses through the restructuring of our operations. If we are successful in raising additional capital, a substantial number of additional shares may be issued and these shares will dilute the ownership interest of our current investors.

If we are unable to sufficiently develop our sales, marketing and distribution capabilities or enter into successful agreements with third parties to perform these functions, we will not be able to fully commercialize our products.

We may not be successful in marketing and promoting our existing product candidates or any other products we develop or acquire in the future. Our sales, marketing and distribution capabilities are very limited. In order to commercialize any products successfully, we must internally develop substantial sales, marketing and distribution capabilities or establish collaborations or other arrangements with third parties to perform these services. We do not have extensive experience in these areas, and we may not be able to establish adequate in-house sales, marketing and distribution capabilities or engage and effectively manage relationships with third parties to perform any or all of such services. To the extent that we enter into co-promotion or other licensing arrangements, our product revenues are likely to be lower than if we directly marketed and sold our products, and any revenues we receive will depend upon the efforts of third parties, whose efforts may not meet our expectations or be successful.

We depend upon the efforts of third parties, such as Baxter for HYLENEX, to promote and sell our current products, but there can be no assurance that the efforts of these third parties will meet our expectations or result in any significant product sales. While these third parties are largely responsible for the speed and scope of sales and marketing efforts, they may not dedicate the resources necessary to maximize product opportunities and our ability to cause these third parties to increase the speed and scope of their efforts may be limited. In addition, sales and marketing efforts could be negatively impacted by the delay or failure to obtain additional supportive clinical trial data for our products. In some cases, third party partners are responsible for conducting these additional clinical trials and our ability to increase the efforts and resources allocated to these trials may be limited.

Most of our current proprietary and partnered products and product candidates rely on the rHuPH20 enzyme.

The rHuPH20 enzyme is a key technological component of Enhanze Technology, our ultrafast insulin program, HYLENEX and other proprietary and partnered products and product candidates. An adverse development for rHuPH20 (e.g., we are unable to obtain sufficient quantities of rHuPH20, we are unable to obtain or maintain material proprietary rights to rHuPH20 or we discover negative characteristics of rHuPH20) would substantially impact multiple areas of our business, including current and potential partnerships, as well as proprietary programs.

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If our proprietary and partnered product candidates do not receive and maintain regulatory approvals, they will not be commercialized, and this failure would substantially impair our ability to generate revenues.

Approval from the FDA is necessary to manufacture and market pharmaceutical products in the United States. Most other countries in which we may do business have similar requirements. To date, two of our product candidates have received regulatory approval from the FDA.

The process for obtaining FDA and other regulatory approvals is extensive, time-consuming and costly, and there is no guarantee that the FDA or other regulatory bodies will approve any new drug applications, or NDAs, that may be filed with respect to any of our proprietary or partnered product candidates, or that the timing of any such approval will be appropriate for our desired product launch schedule and other business priorities, which are subject to change. There are no proprietary or partnered product candidates currently in the NDA approval process, and we and our partners may not be successful in obtaining such approvals for any potential products.

Our proprietary and partnered product candidates may not receive regulatory approvals for a variety of reasons, including unsuccessful clinical trials.

Clinical testing of pharmaceutical products is a long, expensive and uncertain process and the failure or delay of a clinical trial can occur at any stage. Even if initial results of preclinical studies or clinical trial results are promising, we or our partners may obtain different results that fail to show the desired levels of safety and efficacy, or we may not, or our partners may not, obtain applicable regulatory approval for a variety of other reasons. Clinical trials for any of our proprietary or partnered product candidates could be unsuccessful, which would delay or prohibit regulatory approval and commercialization of the product candidates. In the United States, FDA approval can be delayed, limited or not granted for many reasons, including, among others:

- FDA review may not find a product candidate safe or effective enough to merit either continued testing or final approval;
- FDA review may not find that the data from preclinical testing and clinical trials justifies approval, or they may require additional studies that would make it commercially unattractive to continue pursuit of approval;
- the FDA may reject our trial data or disagree with our interpretations of either clinical trial data or applicable regulations;
- the cost of a clinical trial may be greater than what we originally anticipate, and we may decide to not pursue FDA approval for such a trial;
- the FDA may not approve our manufacturing processes or facilities, or the processes or facilities of our key partners, our contract manufacturers or our raw material suppliers;
- the FDA may identify problems or other deficiencies in our existing manufacturing processes or facilities, or the existing processes or facilities of our key partners, our contract manufacturers or our raw material suppliers;
- the FDA may change its formal or informal approval requirements and policies, act contrary to previous guidance, or adopt new regulations; or

the FDA may approve a product candidate for indications that are narrow or under conditions that place the product at a competitive disadvantage, which may limit our sales and marketing activities or otherwise adversely impact the commercial potential of a product.

If the FDA does not approve a proprietary or partnered product candidate in a timely fashion on commercially viable terms, or if development of any product candidate is terminated due to difficulties or delays encountered in the regulatory approval process, it could have a material adverse impact on our business and we will become more dependent on the development of other proprietary

or partnered product candidates and/or our ability to successfully acquire other products and technologies. There can be no assurances that any proprietary or partnered product candidate will receive regulatory approval in a timely manner, or at all.

We anticipate that certain proprietary and partnered products will be marketed, and perhaps manufactured, in foreign countries. The process of obtaining regulatory approvals in foreign countries is subject to delay and failure for many of the same reasons set forth above, as well as for reasons that vary from jurisdiction to jurisdiction. The approval process varies among countries and jurisdictions and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA approval. Foreign regulatory agencies may not provide approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or jurisdictions or by the FDA.

If we or our partners fail to comply with regulatory requirements, regulatory agencies may take action against us or them, which could significantly harm our business.

Any approved products, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for these products, are subject to continual requirements and review by the FDA and other regulatory bodies. Regulatory authorities subject a marketed product, its manufacturer and the manufacturing facilities to continual review and periodic inspections. We will be subject to ongoing regulatory requirements, including required submissions of safety and other post-market information and reports, registration requirements, cGMP regulations, requirements regarding the distribution of samples to physicians and recordkeeping requirements. The cGMP regulations include requirements relating to quality control and quality assurance, as well as the corresponding maintenance of records and documentation. We rely on the compliance by our contract manufacturers with cGMP regulations and other regulatory requirements relating to the manufacture of our products. We and our partners are also subject to state laws and registration requirements covering the distribution of our products. Regulatory agencies may change existing requirements or adopt new requirements or policies. We or our partners may be slow to adapt or may not be able to adapt to these changes or new requirements.

Regulatory requirements applicable to pharmaceutical products make the substitution of suppliers and manufacturers costly and time consuming. We have minimal internal manufacturing capabilities and are, and expect to be in the future, entirely dependent on contract manufacturers and suppliers for the manufacture of our products and for their active and other ingredients. The disqualification of these manufacturers and suppliers through their failure to comply with regulatory requirements could negatively impact our business because the delays and costs in obtaining and qualifying alternate suppliers (if such alternative suppliers are available, which we cannot assure) could delay clinical trials or otherwise inhibit our ability to bring approved products to market, which would have a material adverse effect on our business and financial condition.

Later discovery of previously unknown problems with our proprietary or partnered products, manufacturing processes or failure to comply with regulatory requirements, may result in any of the following:

- restrictions on our products or manufacturing processes;
- warning letters;
- withdrawal of the products from the market;
- voluntary or mandatory recall;

fines;

suspension or withdrawal of regulatory approvals;

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suspension or termination of any of our ongoing clinical trials;

refusal to permit the import or export of our products;

refusal to approve pending applications or supplements to approved applications that we submit;

product seizure; or

injunctions or the imposition of civil or criminal penalties.

For example, because a portion of the HYLENEX manufactured by Baxter was not in compliance with the requirements of the underlying HYLENEX agreements, HYLENEX was voluntarily recalled in May 2010. On August 31, 2010, we announced the completion of our root cause investigation regarding HYLENEX manufacturing, and we have identified a corrective action plan and regulatory strategy to reintroduce HYLENEX to the market. We hope to meet with the FDA in the near future and we will not be able to predict the timing for HYLENEX reintroduction until after meeting with the FDA.

If proprietary or partnered product candidates are approved by regulatory bodies such as the FDA but do not gain market acceptance, our business may suffer and we may not be able to fund future operations.

Assuming that our proprietary or partnered product candidates obtain the necessary regulatory approvals, a number of factors may affect the market acceptance of these existing product candidates or any other products which are developed or acquired in the future, including, among others:

the price of products relative to other therapies for the same or similar treatments;

the perception by patients, physicians and other members of the health care community of the effectiveness and safety of these products for their prescribed treatments;

our ability to fund our sales and marketing efforts and the ability and willingness of our partners to fund sales and marketing efforts;

the degree to which the use of these products is restricted by the approved product label;

the effectiveness of our sales and marketing efforts and the effectiveness of the sales and marketing efforts of our partners;

the introduction of generic competitors; and

the extent to which reimbursement for our products and related treatments will be available from third party payors.

If these products do not gain market acceptance, we may not be able to fund future operations, including the development or acquisition of new product candidates and/or our sales and marketing efforts for our approved products, which would cause our business to suffer.

In addition, our proprietary and partnered product candidates will be restricted to the labels approved by applicable regulatory bodies such as the FDA, and these restrictions may limit the marketing and promotion of the ultimate

products. If the approved labels are restrictive, the sales and marketing efforts for these products may be negatively affected.

Developing and marketing pharmaceutical products for human use involves product liability risks, for which we currently have limited insurance coverage.

The testing, marketing and sale of pharmaceutical products involves the risk of product liability claims by consumers and other third parties. Although we maintain product liability insurance coverage, product liability claims can be high in the pharmaceutical industry and our insurance may not sufficiently cover our actual liabilities. If product liability claims were to be made against us, it is possible that our insurance carriers may deny, or attempt to deny, coverage in certain instances. If a

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lawsuit against us is successful, then the lack or insufficiency of insurance coverage could materially and adversely affect our busin