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**United States
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

**Post-Effective Amendment No. 2 on
FORM S-3 to FORM SB-2**

**REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

HALOZYME THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware
*(State or Other Jurisdiction of Employer
Incorporation or Organization)*

88-0488686
*(I.R.S. Employer
Identification No.)*

**11388 Sorrento Valley Road
San Diego, California 92121
(858) 794-8889**
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

**David A. Ramsay
Halozyme Therapeutics, Inc.
11388 Sorrento Valley Road
San Diego, California 92121
(858) 794-8889**
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copy to:
**Douglas J. Rein, Esq.
DLA Piper LLP (US)
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
(858) 677-1400**

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC:

From time to time as described in the Prospectus.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

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

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a) , may determine.

EXPLANATORY NOTE

Halozyme Therapeutics, Inc., a Delaware corporation, (“Halozyme Delaware”), as successor to Halozyme Therapeutics, Inc., a Nevada corporation (“Halozyme Nevada”), is filing this Post-Effective Amendment No. 1 (this “Amendment”) to Registration Statement No. 333-114776 (the “Registration Statement”) pursuant to Rule 414(d) promulgated under the Securities Act of 1933, as amended (the “Securities Act”), as a result of the registrant’s reincorporation in the State of Delaware from the State of Nevada (the “Reincorporation”). Except as modified by this Amendment, Halozyme Delaware expressly adopts the Registration Statement as its own registration statement effective as of the date of the Reincorporation for all purposes of the Securities Act and the Securities Exchange Act of 1934, as amended.

Halozyme Nevada effected the Reincorporation by merging into its wholly-owned subsidiary Halozyme Delaware pursuant to the terms of an Agreement and Plan of Merger between Halozyme Nevada and our company. At the effective time of the merger:

- each outstanding share of common stock of Halozyme Nevada was converted into one share of common stock of Halozyme Delaware;
- Halozyme Delaware assumed all equity-based award plans and grants previously adopted by Halozyme Nevada (the “Equity Plans”) and reserved for issuance under each Equity Plan a number of its shares of common stock equal to the number of shares of stock which had been reserved under that Equity Plan by Halozyme Nevada;
- each outstanding option or other right to purchase and each outstanding equity-based award relating to shares of Halozyme Nevada common stock became an option or right to purchase, or an award relating to, the same number of shares of Halozyme Delaware common stock, subject to the same terms and conditions, including the per share exercise or conversion price; and
- Halozyme Nevada ceased to exist as a separate legal entity.

The Reincorporation did not result in any material change to the registrant’s business, management, assets, liabilities or net worth. The Halozyme Delaware common stock has continued to be listed on the NASDAQ Global Market under the same ticker symbol, “HALO”.

As a result of the Reincorporation, holders of Halozyme Nevada common stock became holders of Halozyme Delaware common stock, and their rights as holders of Halozyme Delaware common stock are governed by the General Corporation Law of the State of Delaware and Halozyme Delaware’s Certificate of Incorporation and Bylaws. A description of the differences between the rights of holders of Halozyme Nevada common stock and Halozyme Delaware common stock is provided in the registrant’s definitive Proxy Statement filed by Halozyme with the SEC October 11, 2007, under the headings “Significant Differences Between the Corporate Laws of Nevada and Delaware” and “Significant Differences Between Our Current Charter Documents and the Charter Documents of Halozyme Delaware,” which descriptions are incorporated herein by reference and made a part hereof.

This Post-Effective Amendment No. 2 relates to 3,118,375 shares of common stock originally included in the Registration Statement on Form SB-2 (Reg. No. 333-114776). The other shares originally included in the Registration Statement (i) have either been resold by the holders thereof prior to this filing, (ii) are no longer subject to issuance by virtue of the company’s redemption of certain outstanding warrants or (iii) are eligible for resale pursuant to Rule 144 of the Securities Act. Some shares originally included in the Registration Statement may have been resold by the holders thereof prior to this filing pursuant to Rule 144 of the Securities Act.

SUBJECT TO COMPLETION, DATED SEPTEMBER 19, 2008

The information in this prospectus is not complete and may be changed. The selling security holders may not sell these securities under this prospectus until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell nor does it seek an offer to buy these securities in any state where the offer and sale would not be permitted.

PROSPECTUS

3,118,375 Shares

HALOZYME THERAPEUTICS, INC.

Common Stock

This prospectus relates to the sale of up to 3,118,375 shares of our common stock by the selling security holders named in this prospectus. The shares of our common stock offered by the selling security holders through this prospectus are shares previously issued to the selling security holders as well as shares that are issuable upon exercise of warrants. The prices at which the selling security holders may sell the shares will be determined by the prevailing market price for the shares or in negotiated transactions. We are not selling any shares of common stock in this offering and therefore we will not receive any of the proceeds from the sale of these shares. We may receive proceeds from the exercise prices of the warrants if any are exercised by the selling security holders.

Our common stock is listed on The Nasdaq Global Market under the symbol "HALO." On September 16, 2008, the last reported sale price for our common stock was \$7.48 per share.

Investing In Our Common Stock Involves Risks. See "Risk Factors" Beginning On Page 2

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is September ____, 2008.

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You should rely only on the information provided or incorporated by reference in this prospectus. We have not authorized anyone to provide you with additional or different information. This document may only be used where it is legal to sell these securities. You should not assume that any information in this prospectus is accurate as of any date other than the date of this prospectus. Information incorporated by reference in this prospectus is accurate only as of the date of the document incorporated by reference. In this prospectus, unless otherwise indicated, the words “we,” “us,” and “our” refer to Halozyme Therapeutics, Inc. and its subsidiaries and do not refer to the selling security holders.

INDEX TO EXHIBITS

Exhibit Number	Description of Document
5.1	Consent and Opinion of DLA Piper LLP (US)
23.1	Consent of Independent Registered Public Accounting Firm — Ernst & Young LLP
23.2	Consent of Independent Registered Public Accounting Firm — Cacciamatta Accountancy Corporation
23.3	Consent of DLA Piper LLP (US) (contained in Exhibit 5.1)
24.1	Power of Attorney (contained in page II-4)

SUMMARY

The following summary highlights selected information from this prospectus and the information incorporated by reference. Because this is a summary, it does not contain all the information about us that may be important to you. You should read the more detailed information in this prospectus and other documents which are incorporated by reference in this prospectus.

Our Business

We are a biopharmaceutical company developing and commercializing products targeting the extracellular matrix for the drug delivery, metabolism, oncology, and dermatology markets. Our portfolio of products is based on intellectual property covering the family of human enzymes known as hyaluronidases. Hyaluronidases are enzymes (proteins) that break down hyaluronic acid which is a naturally occurring substance in the human body. Our technology is based on our proprietary recombinant human PH20 enzyme, or rHuPH20, a human synthetic version of hyaluronidase that degrades hyaluronic acid, a space-filling, gel-like substance that is a major component of tissues throughout the body, such as skin and bone. The PH20 enzyme is a naturally occurring enzyme that digests hyaluronic acid to temporarily break down the gel, thereby facilitating the penetration and diffusion of other drugs and fluids that are injected under the skin or in the muscle. We have key collaborative agreements with Baxter Healthcare Corporation, or Baxter, and F. Hoffmann-La Roche, Ltd and Hoffmann-La Roche, Inc., or collectively Roche.

Our operations to date have been focused on organizing and staffing Halozyme Therapeutics, Inc. and its operating subsidiary, Halozyme, Inc., as well as acquiring, developing and securing its technology and undertaking product development for our existing products and for our product candidates. We have received FDA approval for two products: Cumulase[®], for use in in-vitro fertilization, and HYLENEX, for use as an adjuvant to increase the absorption and dispersion of other injected drugs and fluids.

In November 2007, we reincorporated from the State of Nevada to the State of Delaware. 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, and in our periodic and current reports filed with the Securities and Exchange Commission ("SEC"). Copies of our current and periodic reports filed with the SEC are available at the SEC Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549, and online at www.sec.gov and our website at www.halozyme.com. Please note that the information on our website is not incorporated by reference in this prospectus.

The Offering

In January 2004, we closed a private financing in which we issued 19,046,721 shares of common stock and warrants to purchase 10,461,943 shares of common stock. We agreed to register the common stock issued and issuable in connection with that financing on behalf of the individuals and entities that participated in the financing. Those individuals and entities are referred to in this prospectus as selling security holders. This prospectus covers the sale of 928,128 shares of common stock that have not been previously sold or are not otherwise eligible for resale pursuant to Rule 144 of the Securities Act and the remaining 2,190,247 shares that are issuable upon exercise of the warrants. We will not receive any proceeds from sales of the shares that are currently outstanding, but we will receive proceeds from the exercise prices of any warrants that are exercised by the selling security holders.

Common stock offered by the selling security holders

3,118,375 Shares

RISK FACTORS

You should carefully consider the following risk factors before purchasing any of our securities. The risks and uncertainties described below are not the only ones we face. There may be additional risks and uncertainties that are not known to us or that we do not consider to be material at this time. If the events described in these risks occur, our business, financial condition and results of operations would likely suffer. This prospectus contains forward-looking statements that involve risks and uncertainties. Our actual results may differ significantly from the results discussed in the forward-looking statements. This section discusses the risk factors that might cause those differences. You should also consider the additional information set forth in our SEC reports on Forms 10-K, 10-Q and 8-K and in the other documents considered a part of this prospectus. See "Where You Can Find More Information."

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.

We have generated only minimal revenue from product sales to date and may never generate significant revenues from future product sales. Even if we do achieve significant revenues from product sales, licensing revenues and milestone payments, we expect to incur significant operating losses over the next several years. We have never been profitable, and we may never become profitable. Through June 30, 2008, we have incurred aggregate net losses of approximately \$86.0 million.

If we do not receive and maintain regulatory approvals for our product candidates, we will not be able to commercialize our products, which would substantially impair our ability to generate revenues.

With the exception of the December 2004 receipt of a CE (European Conformity) Mark, the April 2005 FDA clearance for Cumulase and the December 2005 FDA approval for our spreading agent, HYLENEX, none of our product candidates has received regulatory approval from the FDA or from any similar national regulatory agency or authority in any other country in which we intend to do business. 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.

Other manufacturers have FDA approved products for use as spreading agents, including ISTA Pharmaceuticals, Inc., or ISTA, with an ovine-derived hyaluronidase, Vitrase[®], Amphastar Pharmaceuticals, Inc., or Amphastar, with a bovine-derived hyaluronidase, Amphadase[™], and Primapharm, Inc., or Primapharm, also with a bovine-derived hyaluronidase, Hydase[™]. The FDA has determined that Amphadase, Hydase, HYLENEX and Vitrase are each distinct new chemical entities and hence afforded five years of market exclusivity. The five year market exclusivity precludes identical new chemical entity products from being marketed for a period of five years. For so long as each of these products is established as a distinctly different new chemical entity, the marketing exclusivity granted does not prohibit the marketing of any of these products, including HYLENEX. If the FDA changes its earlier determination that HYLENEX is a distinct new chemical entity, our ability to market HYLENEX will be materially impaired.

The process for obtaining FDA approval is extensive, time-consuming and costly, and there is no guarantee that the FDA will approve any NDAs that we intend to file with respect to any of our product candidates, or that the timing of any such approval will be appropriate for our product launch schedule and other business priorities, which are subject to change. We have not currently begun the NDA approval process for any of our other potential products, and we may not be successful in obtaining such approvals for any of our potential products.

We may not receive regulatory approvals for our product candidates for a variety of reasons, including unsuccessful clinical trials.

Clinical testing of pharmaceutical products is a long, expensive and uncertain process and the failure of a clinical trial can occur at any stage. Even if initial results of pre-clinical studies or clinical trial results are promising, we may obtain different results that fail to show the desired levels of safety and efficacy, or we may not obtain FDA approval for a variety of other reasons. The clinical trials of any of our product candidates could be unsuccessful, which would prevent us from obtaining

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regulatory approval and commercializing the product. FDA approval can be delayed, limited or not granted for many reasons, including, among others:

- FDA officials may not find a product candidate safe or effective enough to merit either continued testing or final approval;
- FDA officials may not find that the data from pre-clinical 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 contract manufacturers or 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 our product candidates in a timely fashion on commercially viable terms, or if we terminate development of any of our product candidates due to difficulties or delays encountered in the regulatory approval process, it will have a material adverse impact on our business and we will be dependent on the development of our other product candidates and/or our ability to successfully acquire other products and technologies. We may not receive regulatory approval of our Chemophase product candidate or any other product candidates, in a timely manner, or at all.

We intend to market certain of our products, and perhaps have certain of our products 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. We may not obtain foreign regulatory 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 fail to comply with regulatory requirements, regulatory agencies may take action against us, 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 FDA requirements, including required submissions of safety and other post-market information and reports, registration requirements, current Good Manufacturing Processes, or 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 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 may be slow to adapt or may not be able to adapt to these changes or new requirements.

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Later discovery of previously unknown problems with our 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;
- 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.

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

We have entered into key 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.

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. We are currently in the process of developing our sales, marketing and distribution capabilities. However, our current capabilities in these areas 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 have entered into non-exclusive distribution agreements with MediCult AS, a Denmark-based distributor, and MidAtlantic Diagnostics, Inc., a New Jersey-based distributor, to market and sell our Cumulase product. We have entered into an exclusive sales and marketing agreement with Baxter to market and sell our HYLENEX product in the United States and

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Puerto Rico. Baxter also has the right to market and sell HYLENEX on an exclusive basis in all territories outside of the United States, if and when we seek and receive the applicable regulatory approvals in those territories.

We depend upon the efforts of these third parties, such as Baxter, 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. Our 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.

If our sole contract manufacturer is unable to manufacture significant amounts of the active pharmaceutical ingredient used in our products, our product development and commercialization efforts could be delayed or stopped.

We have signed a commercial supply agreement with Avid Bioservices, Inc., or Avid, a contract manufacturing organization, to produce bulk recombinant human hyaluronidase for clinical trials and commercial use. Avid will produce the active pharmaceutical ingredient used in each of Cumulase, HYLENEX, Chemophase, and Enhance Technology under cGMP for clinical or commercial scale production and will provide support for the chemistry, manufacturing and controls sections for FDA regulatory filings. Avid has only limited experience manufacturing our active pharmaceutical ingredient batches, and we rely on its ability to successfully manufacture these batches according to product specifications. In addition, as a result of our contractual obligations to Roche, we will be required to significantly scale up our active pharmaceutical ingredient production during the next few years. We do not currently have a significant inventory of the active pharmaceutical ingredient used in our products and product candidates, so if Avid does not maintain its status as an FDA-approved manufacturing facility, is unable to successfully scale up our active pharmaceutical ingredient production, or is unable to manufacture the active pharmaceutical ingredient used in our products and product candidates according to product specifications for any other reason, the commercialization of our products and the development of our product candidates will be delayed and our business will be adversely affected. We have entered into discussions to establish arrangements with an additional manufacturer for these ingredients. We have not yet established, and may not be able to establish, favorable arrangements with additional manufacturers for these ingredients or products should the existing supplies become unavailable or in the event that our sole contract manufacturer is unable to adequately perform its responsibilities. Any delays or interruptions in the supply of materials by Avid could cause the delay of clinical trials and could delay or prevent the commercialization of product candidates that may receive regulatory approval. Such delays or interruptions would have a material adverse effect on our business and financial condition.

If we have problems with the third parties that prepare, fill, finish, and package our product candidates for distribution, our product development and commercialization efforts for these candidates could be delayed or stopped.

In the event that any of our product candidates are used in clinical trials or receive the necessary regulatory approval for commercialization, we rely on third parties to prepare, fill, finish, and package the products prior to their distribution. If we are unable to locate third parties to perform these functions on terms that are economically 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 third-party to prepare, fill, finish, and package Cumulase. This third party has only limited experience manufacturing Cumulase batches and, to date, has not demonstrated a consistent ability to manufacture Cumulase according to product specifications. We have entered into an agreement with another third party to prepare, fill, finish and package Cumulase. We are currently in the technology transfer stage with this third party and expect to initiate commercial manufacturing in 2009. If our third party manufacturers are unable to successfully manufacture Cumulase, we may be unable to supply enough Cumulase product to meet demand. In addition, we currently utilize a subsidiary of Baxter to prepare, fill, finish, and package HYLENEX under a development and supply agreement. Baxter has only limited experience manufacturing HYLENEX batches, and 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.

We may wish to raise funds in the next twelve months, and there can be no assurance that such funds will be available.

During the next twelve months, we may wish to raise additional capital to complete or accelerate the steps required to continue development of our product candidates and to fund general operations. 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 may be required to raise additional capital in the future through the public offering of securities, collaborative agreements, private financings and various other equity or debt financings, including calling outstanding warrants to purchase our common stock.

Currently, warrants to purchase approximately 4.1 million shares of our common stock are outstanding and this amount of outstanding warrants may make us a less desirable candidate for investment for some potential investors. Approximately 1.4 million of our outstanding warrants contain a call feature that, potentially, may allow us to raise funds from the holders of these warrants. We have the ability, at our sole discretion, to call warrants exercisable for up to approximately 1.4 million shares of common stock and, upon such a call, the holders of these warrants have thirty days to decide whether to exercise their warrants at a price of \$1.75 per share or receive \$0.01 from us for each share of common stock that is not exercised.

Considering our stage of development and the nature of our capital structure, 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 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 our product candidates are approved by the FDA but do not gain market acceptance, our business will suffer because we may not be able to fund future operations.

Assuming that we obtain the necessary regulatory approvals, a number of factors may affect the market acceptance of any of our existing product candidates or any other products we develop or acquire in the future, including, among others:

- the price of our 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 our products for their prescribed treatments;
- our ability to fund our sales and marketing efforts;
- the degree to which the use of our products is restricted by the product label approved by the FDA;
- the effectiveness of our sales and marketing efforts; and
- the introduction of generic competitors.

If our 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 ability to market and promote our product candidates will be restricted to the labels approved by the FDA. If the approved labels are restrictive, our sales and marketing efforts 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 made against us, it is possible that our insurance carriers may deny, or attempt to deny, coverage in certain instances. If a lawsuit against us is successful, then the lack or insufficiency of insurance coverage could materially and adversely affect our

business and financial condition. Furthermore, various distributors of pharmaceutical products require minimum product liability insurance coverage before purchase or acceptance of products for distribution. Failure to satisfy these insurance requirements could impede our ability to achieve broad distribution of our proposed products and the imposition of higher insurance requirements could impose additional costs on us.

Our inability to attract, hire and retain key management and scientific personnel, and to recruit qualified independent directors, could negatively affect our business.

Our success depends on the performance of key management and scientific employees with biotechnology experience. Given our small staff size and programs currently under development, we depend substantially on our ability to hire, train, retain and motivate high quality personnel, especially our scientists and management team in this field. If we are unable to retain existing personnel or identify or hire additional personnel, we may not be able to research, develop, commercialize or market our product candidates as expected or on a timely basis and, as a result, our business may be harmed. In addition, we rely on the expertise and guidance of independent directors to develop business strategies and to guide our execution of these strategies. Due to changes in the regulatory environment for public companies over the past few years, the demand for independent directors has increased and it may be difficult for us, due to competition from both like-size and larger companies, to recruit qualified independent directors.

Furthermore, if we were to lose key management personnel, particularly Jonathan Lim, M.D., our president and chief executive officer, or Gregory Frost, Ph.D., our vice president and chief scientific officer, then we would likely lose some portion of our institutional knowledge and technical know-how, potentially causing a substantial delay in one or more of our development programs until adequate replacement personnel could be hired and trained. For example, Dr. Frost has been with us from soon after our inception, and he possesses a substantial amount of knowledge about our development efforts. If we were to lose his services, we would experience delays in meeting our product development schedules. We have not entered into any retention or other agreements specifically designed to motivate officers or other employees to remain with us, other than standard agreements relating to the vesting of stock options that every optionee of the Company must enter into as a condition of receiving an option grant.

We do not have key man life insurance policies on the lives of any of our employees, including Dr. Lim and Dr. Frost.

Risks Related To Ownership of Our Common Stock

Future sales of shares of our common stock upon the exercise of currently outstanding securities or pursuant to our universal shelf registration statement may negatively affect our stock price.

As a result of our January 2004 private financing transaction, we issued warrants to private investors for the purchase of approximately 10.5 million shares of common stock at purchase prices ranging from \$0.77 to \$1.75 per share. Currently, approximately 2.2 million shares of common stock remain issuable upon the exercise of these warrants. As a result of our October 2004 financing transaction, we issued warrants for the purchase of approximately 2.7 million shares of common stock at a purchase price of \$2.25 per share. Currently, approximately 2.0 million shares of common stock remain issuable upon the exercise of these warrants. The exercise of these warrants could result in significant dilution to stockholders at the time of exercise which could negatively affect our stock price.

We currently have the ability, from time to time, to offer and sell up to \$32.5 million of additional equity or debt securities under a currently effective universal shelf registration statement. Sales of substantial amounts of shares of our common stock or other securities under our universal shelf registration statement could lower the market price of our common stock and impair our ability to raise capital through the sale of equity securities. In the future, we may issue additional options, warrants or other derivative securities convertible into 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, 2008 were \$10.50 and \$4.19, 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

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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:

- our failure, or the failure of one of our third party partners, to comply with the terms of our collaboration agreements;
- the termination, for any reason, of any of our collaboration agreements;
- the sale of common stock by any significant shareholder, including, but not limited to, direct or indirect sales by members of 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 FDA approval for any of our products;
- 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 our Chemophase clinical trial due to safety or patient tolerability issues;
- the suspension of our Chemophase 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 the FDA;
- our failure, or the failure of our third party partners, to generate product revenues anticipated by investors;
- problems with our sole API contract manufacturer or our sole fill and finish manufacturer for HYLENEX;
- the exercise of our right to redeem certain outstanding warrants to purchase our common stock;
- the sale of additional debt and/or equity securities by us; and
- the departure of key personnel.

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 recent trading volumes decrease, it may be difficult for stockholders to sell their shares in the public market at any given time at prevailing prices.

Our decision to redeem outstanding warrants may drive down the market price of our stock.

We may have the ability to redeem certain outstanding warrants, under certain conditions, that may be exercised for approximately 1.4 million shares of common stock. The redemption price for these warrants is \$0.01 per share, but the warrant holders have the opportunity to exercise their warrants prior to redemption at the price of \$1.75 per share. If we decide to redeem any portion of our outstanding warrants in the future, some selling security holders may choose to sell outstanding shares of common stock in order to finance the exercise of the warrants prior to their redemption. This pattern of selling may result in a reduction of our common stock's market price.

Risks Related To Our Industry

Compliance with the extensive government regulations to which we are subject is expensive and time consuming and may result in the delay or cancellation of product sales, introductions or modifications.

Extensive industry regulation has had, and will continue to have, a significant impact on our business. All pharmaceutical companies, including ours, are subject to extensive, complex, costly and evolving regulation by the federal government, principally the FDA and, to a lesser extent, the U.S. Drug Enforcement Administration, or DEA, and foreign and state government agencies. The Federal Food, Drug and Cosmetic Act, the Controlled Substances Act and other domestic and foreign statutes and regulations govern or influence the testing, manufacturing, packaging, labeling, storing, recordkeeping, safety, approval, advertising, promotion, sale and distribution of our products. Under certain of these regulations, we and our contract suppliers and manufacturers are subject to periodic inspection of our or their respective facilities, procedures and operations and/or the testing of products by the FDA, the DEA and other authorities, which conduct periodic inspections to confirm that we and our contract suppliers and manufacturers are in compliance with all applicable regulations. The FDA also conducts pre-approval and post-approval reviews and plant inspections to determine whether our systems, or our contract suppliers' and manufacturers' processes, are in compliance with cGMP and other FDA regulations. If we, or our contract supplier, fail these inspections, we may not be able to commercialize our product in a timely manner without incurring significant additional costs, or at all.

In addition, the FDA imposes a number of complex regulatory requirements on entities that advertise and promote pharmaceuticals including, but not limited to, standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet.

We are dependent on receiving FDA and other governmental approvals prior to manufacturing, marketing and shipping our products. Consequently, there is always a risk that the FDA or other applicable governmental authorities will not approve our products, or will take post-approval action limiting or revoking our ability to sell our products, or that the rate, timing and cost of such approvals will adversely affect our product introduction plans or results of operations.

Our suppliers and sole manufacturer are subject to regulation by the FDA and other agencies, and if they do not meet their commitments, we would have to find substitute suppliers or manufacturers, which could delay the supply of our products to market.

Regulatory requirements applicable to pharmaceutical products make the substitution of suppliers and manufacturers costly and time consuming. We have no 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.

We may be required to initiate or defend against legal proceedings related to intellectual property rights, which may result in substantial expense, delay and/or cessation of the development and commercialization of our products.

We rely on patents to protect our intellectual property rights. The strength of this protection, however, is uncertain. For example, it is not certain that:

- our patents and pending patent applications cover products and/or technology that we invented first;
- we were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate our technologies;
- any of our pending patent applications will result in issued patents; and

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- any of our issued patents, or patent pending applications that result in issued patents, will be held valid and infringed in the event the patents are asserted against others.

We currently own or license several U.S. patents and also have pending patent applications. There can be no assurance that our existing patents, or any patents issued to us as a result of our pending patent applications, will provide a basis for commercially viable products, will provide us with any competitive advantages, or will not face third party challenges or be the subject of further proceedings limiting their scope or enforceability. Such limitations in our patent portfolio could have a material adverse effect on our business and financial condition. In addition, if any of our pending patent applications do not result in issued patents, this could have a material adverse effect on our business and financial condition.

We may become involved in interference proceedings in the U.S. Patent and Trademark Office to determine the priority of our inventions. In addition, costly litigation could be necessary to protect our patent position. We also rely on trademarks to protect the names of our products. These trademarks may be challenged by others. If we enforce our trademarks against third parties, such enforcement proceedings may be expensive. We also rely on trade secrets, unpatented proprietary know-how and continuing technological innovation that we seek to protect with confidentiality agreements with employees, consultants and others with whom we discuss our business. Disputes may arise concerning the ownership of intellectual property or the applicability or enforceability of these agreements, and we might not be able to resolve these disputes in our favor.

In addition to protecting our own intellectual property rights, third parties may assert patent, trademark or copyright infringement or other intellectual property claims against us based on what they believe are their own intellectual property rights. If we become involved in any intellectual property litigation, we may be required to pay substantial damages, including but not limited to treble damages, for past infringement if it is ultimately determined that our products infringe a third party's intellectual property rights. Even if infringement claims against us are without merit, defending a lawsuit takes significant time, may be expensive and may divert management's attention from other business concerns. Further, we may be stopped from developing, manufacturing or selling our products until we obtain a license from the owner of the relevant technology or other intellectual property rights. If such a license is available at all, it may require us to pay substantial royalties or other fees.

Future acquisitions could disrupt our business and harm our financial condition.

In order to augment our product pipeline or otherwise strengthen our business, we may decide to acquire additional businesses, products and technologies. As we have limited experience in evaluating and completing acquisitions, our ability as an organization to make such acquisitions is unproven. Acquisitions could require significant capital infusions and could involve many risks, including, but not limited to, the following:

- we may have to issue convertible debt or equity securities to complete an acquisition, which would dilute our stockholders and could adversely affect the market price of our common stock;
- an acquisition may negatively impact our results of operations because it may require us to incur large one-time charges to earnings, amortize or write down amounts related to goodwill and other intangible assets, or incur or assume substantial debt or liabilities, or it may cause adverse tax consequences, substantial depreciation or deferred compensation charges;
- we may encounter difficulties in assimilating and integrating the business, products, technologies, personnel or operations of companies that we acquire;
- certain acquisitions may disrupt our relationship with existing customers who are competitive with the acquired business, products or technologies;
- acquisitions may require significant capital infusions and the acquired businesses, products or technologies may not generate sufficient revenue to offset acquisition costs;
- an acquisition may disrupt our ongoing business, divert resources, increase our expenses and distract our management;

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- acquisitions may involve the entry into a geographic or business market in which we have little or no prior experience; and
- key personnel of an acquired company may decide not to work for us.

If any of these risks occurred, it could adversely affect our business, financial condition and operating results. We cannot assure you that we will be able to identify or consummate any future acquisitions on acceptable terms, or at all. If we do pursue any acquisitions, it is possible that we may not realize the anticipated benefits from such acquisitions or that the market will not view such acquisitions positively.

If third party reimbursement and customer contracts are not available, our products may not be accepted in the market.

Our ability to earn sufficient returns on our products will depend in part on the extent to which reimbursement for our products and related treatments will be available from government health administration authorities, private health insurers, managed care organizations and other healthcare providers.

Third-party payors are increasingly attempting to limit both the coverage and the level of reimbursement of new drug products to contain costs. Consequently, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Third party payors may not establish adequate levels of reimbursement for the products that we commercialize, which could limit their market acceptance and result in a material adverse effect on our financial condition.

Customer contracts, such as with group paying organizations and hospital formularies, will often not offer contract or formulary status without either the lowest price or substantial proven clinical differentiation. If our products are compared to animal-derived hyaluronidases by these entities, it is possible that neither of these conditions will be met, which could limit market acceptance and result in a material adverse effect on our financial condition.

The rising cost of healthcare and related pharmaceutical product pricing has led to cost containment pressures that could cause us to sell our products at lower prices, resulting in less revenue to us.

Any of our products that have been or in the future are approved by the FDA may be purchased or reimbursed by state and federal government authorities, private health insurers and other organizations, such as health maintenance organizations and managed care organizations. Such third party payors increasingly challenge pharmaceutical product pricing. The trend toward managed healthcare in the United States, the growth of such organizations, and various legislative proposals and enactments to reform healthcare and government insurance programs, including the Medicare Prescription Drug Modernization Act of 2003, could significantly influence the manner in which pharmaceutical products are prescribed and purchased, resulting in lower prices and/or a reduction in demand. Such cost containment measures and healthcare reforms could adversely affect our ability to sell our products. Furthermore, individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third party payors or other restrictions could negatively and materially impact our revenues and financial condition. We anticipate that we will encounter similar regulatory and legislative issues in most other countries outside the United States.

We face intense competition and rapid technological change that could result in the development of products by others that are superior to the products we are developing.

We have numerous competitors in the United States and abroad including, among others, major pharmaceutical and specialized biotechnology firms, universities and other research institutions that may be developing competing products. Such competitors include, but are not limited to, Sigma-Aldrich Corporation, ISTA, Amphastar and Primapharm among others. These competitors may develop technologies and products that are more effective, safer, or less costly than our current or future product candidates or that could render our technologies and product candidates obsolete or noncompetitive. Many of these competitors have substantially more resources and product development, manufacturing and marketing experience and capabilities than we do. In addition, many of our competitors have significantly greater experience than we do in undertaking pre-clinical testing and clinical trials of pharmaceutical product candidates and obtaining FDA and other regulatory approvals

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of products and therapies for use in healthcare. Other manufacturers have FDA approved products for use as spreading agents, including ISTA, with an ovine-derived hyaluronidase, Vitrase, Amphastar, with a bovine-derived hyaluronidase, Amphadase, and Primapharm, also with a bovine-derived hyaluronidase, Hydase. The FDA has determined that Amphadase, Hydase, HYLENEX and Vitrase are distinct new chemical entities and hence afforded five years of market exclusivity. The five year market exclusivity precludes identical new chemical entity products from being marketed for a period of five years. As each of these products is established as distinctly different new chemical entities, the marketing exclusivity granted does not prohibit the marketing of the products.

USE OF PROCEEDS

We will not receive proceeds from the sale of shares under this prospectus, but we did receive consideration from the selling security holders at the time they purchased the shares. We may receive proceeds from the exercise price of the warrants if they are exercised by the selling security holders. Assuming the exercise of all the selling security holders' warrants, we would receive gross proceeds of approximately \$3.0 million. We intend to use any proceeds from exercise of the warrants for working capital and general corporate purposes.

SELLING SECURITY HOLDERS

The shares are being offered by certain selling security holders. The selling security holders may from time to time offer and sell pursuant to this prospectus up to an aggregate of 3,118,375 shares of our common stock now owned by them or issuable to them upon the exercise of warrants. The selling security holders may, from time to time, offer and sell any or all of the shares that are registered under this prospectus. Because the selling security holders are not obligated to sell their shares, and because the selling security holders may also acquire publicly traded shares of our common stock, we cannot estimate how many shares the selling security holders will own after the offering.

Shares held by a selling security holder that are otherwise eligible for resale pursuant to Rule 144 of the Securities Act are not included in this prospectus.

None of the selling security holders has ever held an office, been a director or had any other material relationship with Halozyne or any of its predecessor companies.

Pursuant to the stock purchase agreements with the selling security holders, all expenses incurred with respect to the registration of the common stock will be borne by us, but we will not be obligated to pay any underwriting fees, discounts, commissions or other expenses incurred by them in connection with the sale of such shares.

The following table sets forth, with respect to the selling security holders: (i) the number of shares of common stock covered by this prospectus, (ii) the number of shares of common stock covered by this prospectus that are issuable upon exercise of the warrants, (iii) the total shares of common stock covered by this prospectus, (iv) the total number of shares of common stock beneficially owned but not covered by this prospectus*, (v) the total number of shares of company stock beneficially owned by such selling security holders as of September 1, 2008*, and (vi) the percentage of shares of common stock beneficially owned as of September 1, 2008, based upon 80,478,914 shares of common stock outstanding as of that date.

* Each selling security holder's beneficial ownership total reflects shares owned beneficially as of August 12, 2004 as adjusted by (i) warrant redemptions and (ii) the sale of registered shares from that date through September 15, 2008 pursuant to prior versions of this prospectus. Such totals do not include any other shares that were purchased or sold unless such purchases and sales were reported in public filings made with the Securities and Exchange Commission.

Security Holders	Shares of Common Stock Being Registered	Shares of Common Stock Issuable Upon Exercise of Warrants	Total Shares of Common Stock Equivalents Being Registered	Shares of Common Stock Beneficially Owned But NOT Being Registered	Total Shares of Common Stock Beneficially Owned	Total Beneficial Ownership%
Anthony Salandra	—	57,223	57,223	72,873	130,096	0.16%
Asia Pacific Imports	—	11,250	11,250	63,750	75,000	0.09%
Autry Qualified Interest Trust	—	45,500	45,500	254,500	300,000	0.37%
Bonanza Master Fund, LTD	136,300	—	136,300	1,789,286	1,925,586	2.39%
Darren Blanton	322,788	—	322,788	1,017,074	1,339,862	1.66%
David Hochman	—	2,350	2,350	—	2,350	0.00%
Franklin H. Nyi	—	18,200	18,200	101,800	120,000	0.15%
Gene Salkind, MD	—	36,400	36,400	328,600	365,000	0.45%
Harvest International	107,596	—	107,596	107,596	215,192	0.27%
Henri Talerman	—	15,000	15,000	95,000	110,000	0.14%
Jacqueline Autry	—	9,100	9,100	50,900	60,000	0.07%
Jerome Morgan	—	2,000	2,000	11,200	13,200	0.02%
Jesse Grossman	—	442,891	442,891	1,318,717	1,761,608	2.18%
John Paul DeJoria	—	18,200	18,200	51,800	70,000	0.09%
John Long	—	35,870	35,870	—	35,870	0.04%
Jonathan Spanier	251,917	—	251,917	1,480,819	1,732,736	2.15%
Keith Granirer	—	1,713	1,713	7,500	9,213	0.01%
Ken Rickel	—	267,442	267,442	496,042	763,484	0.95%
Ken Y. Leung	—	18,200	18,200	91,800	110,000	0.14%
Kingsbridge Capital	22,100	—	22,100	34,400	56,500	0.07%
Laura Stone	—	1,650	1,650	11,765	13,415	0.02%
Lawrence Diamant	—	812	812	3,938	4,750	0.01%
Linda May Stone	15,000	—	15,000	41,400	56,400	0.07%
Louis F. Burke PC Retirement Trust	—	4,600	4,600	22,900	27,500	0.03%
Michael P. Marcus	—	18,200	18,200	20,000	38,200	0.05%
Nadine Smith	69,327	100	69,427	44,962	114,389	0.14%

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Security Holders	Shares of Common Stock Being Registered	Shares of Common Stock Issuable Upon Exercise of Warrants	Total Shares of Common Stock Equivalents Being Registered	Shares of Common Stock Beneficially Owned But NOT Being Registered	Total Shares of Common Stock Beneficially Owned	Total Beneficial Ownership%
Peter Geddes	3,100	332,119	335,219	1,882,718	2,217,937	2.74%
Peter Geddes Custodian for Campbell	—	11,450	11,450	57,300	68,750	0.09%
Geddes under CUTMA, age 21						
Peter Geddes Custodian for Lily	—	11,450	11,450	57,300	68,750	0.09%
Geddes under CUTMA, age 21						
Richard Genovese Roth Capital Partners, LLC	—	571,852	571,852	1,393,786	1,965,638	2.43%
Steven S. Vender	—	94,400	94,400	41,900	136,300	0.17%
TBG America Inc.	—	10,275	10,275	56,600	66,875	0.08%
The Ward Family Foundation	—	18,200	18,200	—	18,200	0.02%
Vega Investments Inc.	—	27,300	27,300	152,700	180,000	0.22%
Vertical Ventures, LLC	—	47,300	47,300	30,700	78,000	0.10%
William F. Miller III	—	45,500	45,500	—	45,500	0.06%
Total	928,128	2,190,247	3,118,375	11,315,426	14,433,801	17.89%

Subject to applicable exceptions set forth by the Securities and Exchange Commission, transferees, pledgees, donees or successors to the selling security holders named in the prospectus may not offer and sell securities pursuant to the prospectus unless we supplement or amend the prospectus to reflect the required information concerning such transferees, pledgees, donees or successors.

PLAN OF DISTRIBUTION

The selling security holders and any of their pledgees, assignees and successors-in-interest may, from time to time, sell all or any part of their shares of common stock offered hereby on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling security holders may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- broker-dealers may agree with the selling security holders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling security holders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus. The selling security holders may also engage in short sales against the box, puts and calls and other transactions in our securities or derivatives of our securities, and may sell or deliver shares in connection with these trades. The selling security holders may pledge their shares to their brokers under the margin provisions of customer agreements. If a selling security holder defaults on a margin loan, the broker may, from time to time, offer and sell the pledged shares.

Broker-dealers engaged by the selling security holders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling security holders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling security holders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The selling security holders and any broker-dealers or agents that are involved in selling the shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. Any selling security holders that are broker-dealers or broker-dealer affiliates will be deemed to be “underwriters” within the meaning of the Securities Act in connection with any sales of the shares by them. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Of the selling security holders Roth Capital Partners, LLC is a broker-dealer.

Because selling security holders may be deemed to be “underwriters” within the meaning of Section 2(11) of the Securities Act, the selling security holders will be subject to the prospectus delivery requirements of the Securities Act and the rules promulgated thereunder. We have informed the selling security holders that the anti-manipulative provisions of Regulation M promulgated under the Exchange Act may apply to their sales in the market.

We are required to pay all fees and expenses (excluding selling expenses) incident to the registration of the shares being registered herein, including fees and disbursements of counsel to the selling security holders. We have agreed to indemnify certain of the selling security holders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

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After being notified by a selling security holder that any material arrangement has been entered into with a broker-dealer or underwriter for the sale of shares through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker, dealer or underwriter, we will file a supplement to this prospectus, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such selling security holder and of the participating broker-dealer(s) or underwriter(s), (ii) the number of shares involved, (iii) the price at which such shares were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s) or underwriter(s), where applicable, (v) that such broker-dealer(s) or underwriter(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus and (vi) other facts material to the transaction. Individuals and entities who receive shares from the selling security holders as a gift or in connection with a pledge may sell up to 500 of such shares pursuant to this prospectus.

LEGAL MATTERS

The validity of the shares of common stock being sold in this offering and other legal matters relating to the offering has been passed upon for us by DLA Piper LLP (US), San Diego, California.

EXPERTS

The consolidated financial statements of Halozyme Therapeutics, Inc. appearing in Halozyme Therapeutics, Inc.'s Annual Report (Form 10-K) as of and for the years ended December 31, 2007 and 2006, and the effectiveness of Halozyme Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2007, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The consolidated financial statements of Halozyme Therapeutics, Inc. as of December 31, 2005, and for the year then ended, have been incorporated by reference herein and in the Registration Statement in reliance upon the report of Cacciamatta Accountancy Corporation, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We file proxy statements and annual, quarterly and special reports and other information with the SEC. You can inspect and copy the registration statement as well as the reports, proxy statements and other information we have filed with the SEC at the public reference room maintained by the SEC at 450 Fifth Street, N.W., Washington, D.C. You can call the SEC at 1-800-SEC-0330 for further information about the public reference rooms. We are also required to file electronic versions of these documents with the SEC, which may be accessed from the SEC's Internet site at <http://www.sec.gov> or at our website <http://www.halozyme.com>.

The SEC requires us to "incorporate by reference" certain of our publicly-filed documents into this prospectus, which means that information included in those documents is considered part of this prospectus. Information that we file with the SEC after the effective date of this prospectus will automatically update and supersede this information, as well as the other information contained in this prospectus. In addition, we also incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 after the date of the filing of this registration statement, until such time as the effectiveness of this registration statement is terminated.

The following documents filed with the SEC are incorporated by reference in this prospectus:

1. Our Annual Report on Form 10-K for the year ended December 31, 2007, filed with the SEC on March 14, 2008.
2. Our Quarterly Report on Form 10-Q for the periods ended March 31, 2008, filed with the SEC on May 9, 2008.
3. Our Quarterly Report on Form 10-Q for the periods ended June 30, 2008, filed with the SEC on August 8, 2008.
4. Our Current Reports on Form 8-K filed with SEC on February 8, 2008; March 19, 2008; April 21, 2008; and August 21, 2008.
5. Our definitive Proxy Statement on Schedule 14A, including a description of the differences between the rights of holders of Halozyme Nevada common stock and Halozyme Delaware common stock, filed with the SEC on October 11, 2007.
6. Our Post-Effective Amendment No. 1 to Registration Statement on Form S-3, file No. 333-125731, including the description of our common stock contained therein, filed with the SEC on September 19, 2008.
7. All of the filings pursuant to the Securities Exchange Act that we may make prior to the effectiveness of this registration statement, and prior to the termination of the offering contemplated by this prospectus.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference. You should direct any requests for documents to David Ramsay, Chief Financial Officer, 11388 Sorrento Valley Road, San Diego, California 92121, telephone: (858) 794-8889.

DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “anticipates,” “estimates,” “plans,” “projects,” “continuing,” “ongoing,” “expects,” “management believes,” “we believe,” “we intend” and similar words or phrases. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors listed under the section entitled “Risk Factors.”

Because the factors referred to in the preceding sentence could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements we make, you should not place undue reliance on any such forward-looking statements. Further, any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

**3,118,375 SHARES OF
COMMON STOCK
HALOZYME THERAPEUTICS, INC.**

**PROSPECTUS
SEPTEMBER __, 2008**

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The expenses in connection with the sale of the securities being registered are set forth in the following table (all amounts except the registration fee are estimated) and all expenses will be borne by the Registrant:

SEC Registration Fee	\$ 15,740
Printing and Engraving Expenses	\$ 5,000
Legal Fees and Expenses	\$ 20,000
Accounting Fees and Expenses	\$ 10,000
Miscellaneous	\$ 1,260
Total	\$ 53,000

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Our bylaws provide for the indemnification of our directors, officers, employees and agents to the fullest extent permitted by the Delaware General Corporation Law (“DGCL”).

Section 145 of the DGCL provides that a corporation may indemnify any person made a party to an action (other than an action by or in the right of the corporation) by reason of the fact that he or she was a director, officer, employee or agent of the corporation or was serving at the request of the corporation against expenses (including attorneys’ fees), judgments, fines, and amounts paid in settlement actually and reasonably incurred by him or her in connection with such action if he or she acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the corporation and, with respect to any criminal action (other than an action by or in the right of the corporation), has no reasonable cause to believe his or her conduct was unlawful. We have entered into indemnification agreements with our officers and directors.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, we have been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

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ITEM 16. EXHIBITS

Exhibit Number	Description of Document
5.1	Consent and Opinion of DLA Piper LLP (US)
23.1	Consent of Independent Registered Public Accounting Firm — Ernst & Young LLP
23.2	Consent of Independent Registered Public Accounting Firm — Cacciamatta Accountancy Corporation
23.3	Consent of DLA Piper LLP (US) (contained in Exhibit 5.1)
24.1	Power of Attorney (contained in page II-4)

ITEM 17. UNDERTAKINGS

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933 (the “Securities Act”);

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the “Calculation of Registration Fee” table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

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- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) The undersigned Registrant hereby undertakes to deliver or cause to be delivered with the prospectus, to each person to whom the prospectus is sent or given, the latest annual report to security holders that is incorporated by reference in the prospectus and furnished pursuant to and meeting the requirements of Rule 14a-3 or Rule 14c-3 under the Securities Exchange Act of 1934; and, where interim financial information required to be presented by Article 3 of Regulation S-X are not set forth in the prospectus, to deliver, or cause to be delivered to each person to whom the prospectus is sent or given, the latest quarterly report that is specifically incorporated by reference in the prospectus to provide such interim financial information.

(d) Insofar as indemnification for liabilities under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Post-Effective Amendment No. 2 to the registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of San Diego, State of California, on September 18, 2008.

HALOZYME THERAPEUTICS, INC.

BY: /s/ Jonathan E. Lim, M.D.

Jonathan E. Lim, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Jonathan E. Lim and David A. Ramsay, and each of them, his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities including his or her capacity as a director and/or officer of Halozyme Therapeutics, Inc., to sign any and all amendments (including post-effective amendments) to this registration statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
_____ /s/ Jonathan E. Lim, M.D. Jonathan E. Lim, M.D.	President and Chief Executive Officer (Principal Executive Officer), Director	September 18, 2008
_____ /s/ David A. Ramsay David A. Ramsay	Secretary and Chief Financial Officer (Principal Financial and Accounting Officer)	September 18, 2008
_____ /s/ Gregory I. Frost, Ph.D. Gregory I. Frost, Ph.D.	Vice President and Chief Scientific Officer, Director	September 18, 2008
_____ /s/ Kenneth J. Kelley Kenneth J. Kelley	Chairman of the Board of Directors	September 18, 2008
_____ /s/ Robert L. Engler, M.D. Robert L. Engler, M.D.	Director	September 18, 2008
_____ /s/ Kathryn E. Falberg Kathryn E. Falberg	Director	September 18, 2008
_____ /s/ Randal J. Kirk Randal J. Kirk	Director	September 18, 2008

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Signature	Title	Date
<hr/> <i>/s/ Connie Matsui</i> Connie Matsui	Director	September 18, 2008
<hr/> <i>/s/ John S. Patton, Ph.D.</i> John S. Patton, Ph.D.	Director	September 18, 2008
<hr/> <i>/s/ Steven T. Thornton</i> Steven T. Thornton	Director	September 18, 2008

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DLA Piper LLP (US)
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
www.dlapiper.com

T 858.677.1400
F 858.677.1401

September 19, 2008

Halozyme Therapeutics, Inc.
11388 Sorrento Valley Road
San Diego, California 92121

Ladies and Gentlemen:

We have acted as counsel to Halozyme Therapeutics, Inc., a Delaware corporation (the “*Company*”), in connection with the filing on the date hereof of a Post-Effective Amendment No. 2 on Form S-3 to the Registration Statement on Form SB-2 filed on April 23, 2004, as amended (the “*Registration Statement*”), under the Securities Act of 1933, as amended (the “*Securities Act*”). The Registration Statement relates to the registration of a total of 3,118,375 shares of the Company’s common stock, par value \$0.001 per share (the “*Shares*”), for resale by the stockholders identified in the Registration Statement, (i) 928,128 of which are issued and outstanding and (ii) up to 2,190,247 of which are issuable by the Company upon the exercise of outstanding warrants (the “*Warrant Shares*”).

We have examined all instruments, documents and records which we deemed relevant and necessary for the basis of our opinion hereinafter expressed. In such examination, we have assumed the genuineness of all signatures and the authenticity of all documents submitted to us as originals and the conformity to the originals of all documents submitted to us as copies. We express no opinion concerning any law other than the corporation law of the State of Delaware and the federal law of the United States. As to matters of Delaware corporation law, we have based our opinion solely upon our examination of such laws and the rules and regulations of the authorities administering such laws, all as reported in standard, unofficial compilations.

Based on such examination, we are of the opinion that the Shares (excluding the Warrant Shares) have been duly authorized and validly issued, and are fully paid and nonassessable and, if, as and when the Warrant Shares are issued and delivered by the Company pursuant to the terms of each warrant, including, without limitation, payment in full of the applicable consideration, the Warrant Shares will be duly authorized, validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement and the reference to us under the caption “Legal Matters” in the prospectus included in the Registration Statement. In giving this consent, we do not admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Securities and Exchange Commission promulgated thereunder.

This opinion letter is given to you solely for use in connection with the registration for resale of the Shares in accordance with the prospectus included in the Registration Statement and is not to be relied upon for any other purpose. Our opinion is expressly limited to the matters set forth above, and we render no opinion, whether by implication or otherwise, as to any other matters relating to the Company, the Shares or the Registration Statement.

Very truly yours,

/s/ DLA PIPER LLP (US)

DLA Piper LLP (US)

Consent of Independent Registered Public Accounting Firm — Ernst & Young LLP

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Post Effective Amendment No. 2 on Form S-3 to Form SB-2 No. 333-114776) and related Prospectus of Halozyme Therapeutics, Inc. for the registration of 3,118,375 shares of its common stock and to the incorporation by reference therein of our reports dated March 12, 2008, with respect to the consolidated financial statements of Halozyme Therapeutics, Inc., and the effectiveness of internal control over financial reporting of Halozyme Therapeutics, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2007, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

San Diego, California
September 16, 2008

**Consent of Independent Registered Public Accounting Firm —
Cacciamatta Accountancy Corporation**

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Post Effective Amendment No. 2 on Form S-3 to Form SB-2 No. 333-114776) and related Prospectus of Halozyme Therapeutics, Inc. for the registration of 3,118,375 shares of its common stock and to the incorporation by reference therein of our reports dated March 12, 2006, with respect to the consolidated financial statements of Halozyme Therapeutics, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2007, filed with the Securities and Exchange Commission.

/s/ Cacciamatta Accountancy Corporation

Santa Ana, California
September 19, 2008