

BUILDING ON OUR SUCCESS

**NASTECH ANNUAL REPORT 2005**

#### **OUR MISSION**

To develop and commercialize innovative pharmaceutical products based on active delivery molecules in order to effectively transport therapeutic drugs to their disease targets.

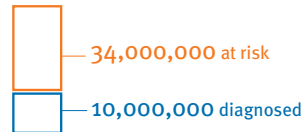
#### **OUR VISION**

To improve human health through the development of products that solve complex drug delivery problems and provide superior therapeutic options to patients in need.

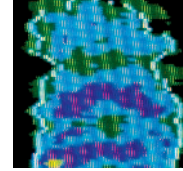
*On the cover:* The figure on the left and extending to the back cover is a molecular model of an insulin hexamer. Insulin nasal spray for treatment of diabetes is one example of Nastech's development of non-invasive peptide and protein therapeutics. The figure on the right is a double-helix oligonucleotide representing Nastech's work in developing small interfering RNA therapeutics.



## OSTEOPOROSIS



Osteoporosis is a major public health threat for an estimated 44 million Americans, or 55 percent of the people 50 years of age and older. In the U.S., 10 million individuals are estimated to already have the disease and almost 34 million more are estimated to have low bone mass, placing them at increased risk for osteoporosis.



ability to systemically deliver a siRNA therapeutic against TNF-alpha as a treatment for rheumatoid arthritis (RA).

### OUR TACTICS: PROVIDE VALUE TO A PARTNER ON NUMEROUS FRONTS

During a development program, Nastech creates value for a partner in numerous areas including formulation, non-clinical and clinical testing, regulatory, manufacturing, and intellectual property. Because we offer all these components to a potential partner, we have been successful in establishing multiple partnerships that provide both significant near-term funding and future revenue opportunities.

#### 2005 PROGRAM HIGHLIGHTS:

##### Parathyroid Hormone (PTH<sub>1-34</sub>) Nasal Spray

Throughout 2005, we added value to our PTH<sub>1-34</sub> nasal spray program through our efforts in formulation science, non-clinical and clinical development, regulatory strategy and intellectual property. We initiated three-month non-clinical safety studies and completed two clinical trials of this promising product candidate. We discussed with the FDA the use of a 505(b)(2) regulatory pathway, which we believe will streamline the regulatory process and speed this compound to market. We then entered into discussion with numerous potential partners, and in February 2006 signed a worldwide collaboration with Procter & Gamble Pharmaceuticals, Inc. (P&G) to develop and commercialize PTH<sub>1-34</sub> nasal spray for the treatment of osteoporosis. With a potential value of \$577 million, this collaboration is one of the largest single-product collaborations in the biotechnology industry over the last several years. The \$577 million deal included \$10 million in an up-front payment, \$22 million in milestone payments expected during 2006, escalating double-digit royalties and reimbursement of development costs. We also have the potential for manufacturing revenue in addition to co-promotion rights for the product in the United States.

The PTH<sub>1-34</sub> program illustrates one part of our business strategy, identifying and pursuing relatively low-risk opportunities from a development, regulatory and cost perspective. These efforts are focused on developing non-invasive alternatives to approved products with significant markets. For example, the efficacy and safety of the approved PTH<sub>1-34</sub> injectable product is known, and the 2005 annual sales for this product were \$389 million, with continuing growth expected in the future. We believe that P&G's osteoporosis expertise and marketing capabilities will allow us to realize the full value of PTH<sub>1-34</sub> nasal spray upon commercialization.

##### Insulin Nasal Spray

We are developing an insulin nasal spray as a potential alternative to injected or inhaled insulin for the treatment of diabetes. Diabetes, the fifth leading cause of death by disease in the United States, is a tremendous and growing health problem.

We believe that an insulin nasal spray could provide millions of diabetics with a non-invasive approach to managing their blood sugar, and may encourage many patients who have poor glucose control but who are reluctant to use an injected therapy to begin insulin treatment.

Recent FDA advisory panel recommendations for the approval of an inhaled form of insulin established the safety and efficacy criteria of non-invasive formulations of insulin. We intend to use the criteria to guide the development of intranasal insulin, which may help us to advance this program more efficiently.

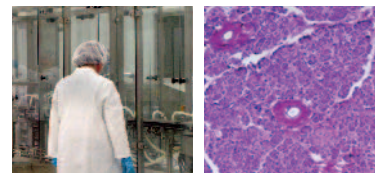
##### Calcitonin-Salmon Nasal Spray

Nastech has developed calcitonin-salmon nasal spray as a generic formulation of Novartis' branded osteoporosis product, Miacalcin® calcitonin-salmon nasal spray. Nastech's product is partnered with Par Pharmaceutical for commercialization.

## OBESITY



Currently, more than 64% of U.S. adults are either overweight or obese, according to results from the 1999–2000 National Health and Nutrition Examination Survey (NHANES). This figure represents a 14% increase in the prevalence rate from NHANES III (1988–94) and a 36% increase from NHANES II (1976–80). (Prevalence is the percentage of the population that falls into the designated category.)



Nastech's Abbreviated New Drug Application (ANDA) for this product was accepted by the FDA in 2004 and is currently undergoing FDA review. In 2005, we successfully completed a FDA Pre-Approval Inspection (PAI) of our calcitonin-salmon nasal spray manufacturing facility in Hauppauge, New York and, in February 2006, completed the PAI for our facility in Bothell, Washington. Successful completion of these FDA inspections provides Nastech with two FDA-inspected manufacturing facilities and positions us to meet the forecasted demand for calcitonin-salmon nasal spray upon FDA approval and commercial launch.

### Peptide YY<sub>3-36</sub> Nasal Spray

Peptide YY<sub>3-36</sub> (PYY) is a naturally occurring hormone that is believed to act as a satiety signal, telling the brain that you have eaten enough. Thus PYY represents a novel approach for treating obesity. In 2005, clinical trials with PYY nasal spray for obesity were completed under a collaboration with Merck & Co. In March 2006, we reacquired the rights to the PYY program from Merck. We believe that the preclinical and clinical trial results to date support the continued development of this important product candidate for the treatment of obesity, and we remain committed to the further advancement of the PYY clinical program. The most recent trial, conducted by Merck, indicates that Nastech's formulation is capable of delivering PYY via nasal administration to the blood stream with an acceptable nasal safety profile. The reacquisition will allow us to move aggressively to conduct additional dose-ranging studies and, if successful, to progress into additional Phase II clinical trials. We will then seek a new commercial partnership for PYY with a major pharmaceutical company that has a strong presence in metabolic diseases and that is capable of conducting late-stage clinical development and worldwide commercialization.

### Feasibility Partnerships

We have entered into several feasibility partnerships with leading biotechnology and pharmaceutical companies based on our innovative technology for the non-invasive delivery of peptides and proteins. Partners typically approach Nastech with compounds for which our advanced delivery technologies could improve safety, ease of use, patient compliance, or enhance product lifecycle such as extending patent protection. Nastech's goal is to create a product with improved marketability.

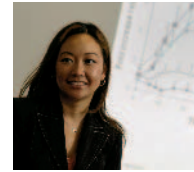
During 2005, our feasibility programs included a treatment for Type II diabetes, a novel obesity target, an intranasal formulation of an erythropoietin (EPO) receptor agonist for treating anemia and a product for treating Alzheimer's disease. Additionally, in March 2006, we entered into a multi-compound agreement with Novo Nordisk A/S, a leader in therapeutics for metabolic diseases, targeting undisclosed indications. All of these programs address multi-billion dollar markets and present significant opportunities for Nastech and our partners. Success in these studies would provide us with the opportunity to expand these partnerships into significant product development collaborations.

### siRNA Program

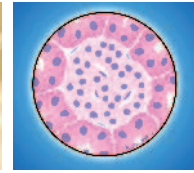
Nastech is building on its success and expertise in developing novel large-molecule drug delivery technologies to enable new therapeutic modalities. Toward this end, we made significant progress in our RNAi program during 2005 and early 2006.

We were the first to demonstrate successful *in vivo* systemic delivery of a siRNA therapeutic, resulting in significant clinical effect at pharmacologic doses in a preclinical model of rheumatoid arthritis (RA). The data demonstrates that our siRNA therapeutic approach reduces the expression of the target protein and highlights the potential of our proprietary delivery peptides to get siRNA therapeutics to their site of action.

## DIABETES



There are 20.8 million people in the United States, or 7% of the population, who have diabetes. While an estimated 14.6 million have been diagnosed with diabetes, unfortunately, 6.2 million people (or nearly one-third) are unaware that they have the disease.



In 2005, we enhanced our siRNA therapeutics program by in-licensing a portfolio of intellectual property from Alnylam Pharmaceuticals, Inc. covering compositions and uses of siRNA therapeutics for the treatment of RA. We further strengthened our program in February 2006 through the acquisition of RNAi intellectual property and other RNAi technologies from Galenea Corp. and MIT for the development of RNAi therapeutics against respiratory viral infections and respiratory diseases. This transaction enables us to expand our RNAi therapeutics pipeline by initiating programs targeting influenza and potentially other respiratory diseases.

In March 2006, we presented *in vitro* and *in vivo* results of studies that use siRNAs specifically designed to target conserved regions of the influenza viral genome. We believe that targeting the conserved regions could enable a siRNA therapeutic to be effective against both current and future strains of the influenza virus. A therapeutic that is broadly effective against different virus strains is essential for the development of a drug that could be stockpiled for rapid mobilization during an influenza pandemic, which has become an impending threat to worldwide public health. *In vitro* screening results identified highly potent siRNAs that were effective against representative human and avian influenza strains, including the H5N1 avian influenza virus.

Furthermore, *in vivo* results demonstrate that direct-to-lung and intravenous administrations of selected proprietary formulations of siRNAs effectively inhibit influenza viral production in a non-clinical model, resulting in a 200-fold reduction of viral concentration in the blood. We are very encouraged by these results and will make every effort to rapidly advance the development of siRNA products to address this critical global health concern.

### BUILDING FOR THE FUTURE

Our success in 2005 sets a foundation for achieving several key objectives in 2006. Our RNAi program will move toward the clinic while we continue building capabilities that support expansion of this technology into additional therapeutic areas. Additionally, we anticipate making progress with our insulin and PYY nasal spray programs. Working with partners, we expect to advance the development of our PTH<sub>1-34</sub> nasal spray program while executing feasibility programs that create additional opportunities for collaboration. Finally, in terms of products, we will continue to work toward FDA approval and product launch of calcitonin-salmon nasal spray.

We will continue managing our assets and financial resources prudently, in a manner that enables strong financial performance today while supporting our long-term growth potential. We have been successful in leveraging partnerships to fund the development of promising internal programs while retaining a substantial portion of the long-term value of partnered programs through milestone payments, product sales royalties and manufacturing revenues. Establishing high-value collaborations will remain a critical component of our business strategy.

I would like to take this opportunity to recognize the contributions and commitment of everyone at Natestech. Working together, we can achieve our goal of building a successful specialty pharmaceutical company, creating value for patients and our shareholders. As much as we have achieved in 2005, I am confident that our momentum and achievements will continue throughout 2006 and beyond.

**Steven C. Quay, M.D., Ph.D.**

Chairman, President and  
Chief Executive Officer



May 2006

#### **BOARD OF DIRECTORS**

Steven C. Quay, M.D., Ph.D.  
*Chairman of the Board, President  
and Chief Executive Officer*

Susan B. Bayh, J.D.  
J. Carter Beese, Jr.  
Alexander D. Cross, Ph.D.  
Ian R. Ferrier, M.D.  
Myron Z. Holubiak  
Leslie D. Michelson  
John V. Pollock  
Gerald T. Stanewick  
Bruce R. Thaw  
Devin N. Wenig

#### **EXECUTIVE MANAGEMENT**

Steven C. Quay, M.D., Ph.D.  
*Chairman of the Board, President  
and Chief Executive Officer*

Philip C. Ranker  
*Chief Financial Officer and Corporate Secretary*

Gordon C. Brandt, M.D.  
*Executive Vice President, Clinical Research  
and Medical Affairs*

Paul H. Johnson, Ph.D.  
*Senior Vice President, Research & Development  
and Chief Scientific Officer*

Timothy M. Duffy  
*Executive Vice President, Marketing  
and Business Development*

David E. Wormuth  
*Senior Vice President, Operations*

#### **FORWARD-LOOKING STATEMENT**

This Annual Report contains forward-looking statements and readers should carefully review the risk factors in Form 10-K included herein.

#### **REGISTRAR AND TRANSFER AGENT**

American Stock Transfer & Trust Co.  
59 Maiden Lane  
New York, N.Y. 10038  
Toll-free: 1-877-777-0800

#### **LEGAL COUNSEL**

Pryor Cashman Sherman & Flynn LLP  
410 Park Avenue  
New York, N.Y. 10022

#### **INDEPENDENT REGISTERED PUBLIC ACCOUNTANTS**

KPMG LLP  
801 Second Avenue  
Seattle, W.A. 98104

#### **PUBLIC RELATIONS**

Noonan Russo  
200 Madison Avenue, 7th Floor  
New York, N.Y. 10016  
212-845-4235

#### **STOCK LISTING**

The Company's Common Stock is traded on the Nasdaq National Market System under the symbol NSTK.

#### **ANNUAL MEETING**

June 13, 2006  
9:00 a.m.  
The University Club  
1 West 54th Street  
New York, N.Y. 10019

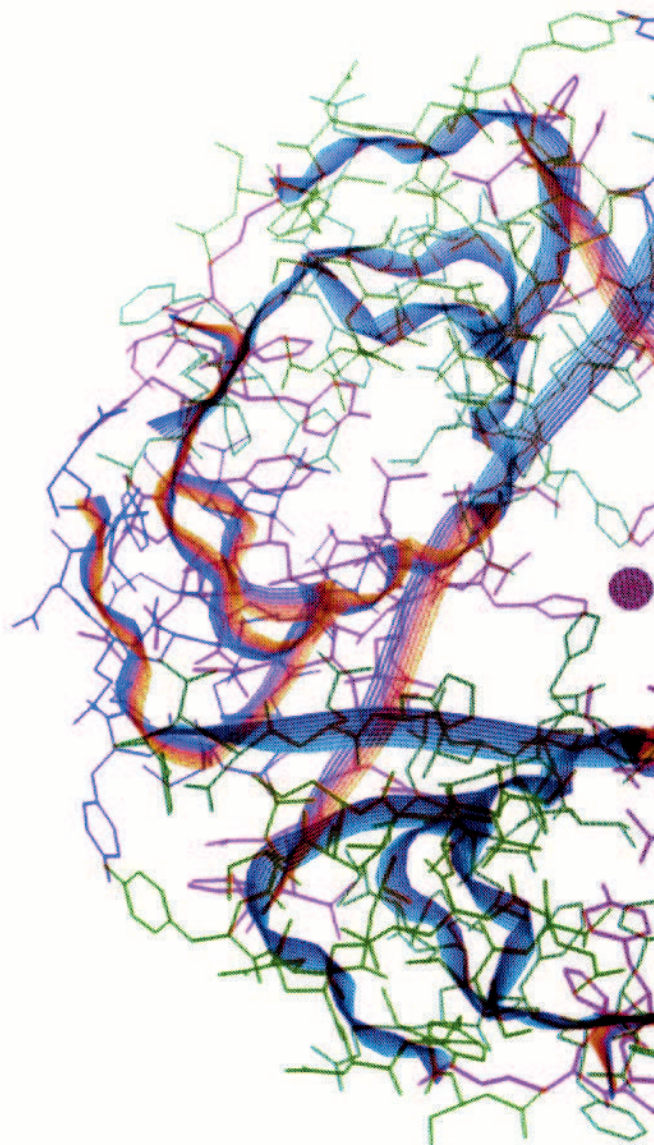
#### **ANNUAL REPORT ON FORM 10-K**

The Company's Annual Report on Form 10-K, filed with the Securities and Exchange Commission, is available without charge by writing, phoning or visiting our website at [www.nastech.com](http://www.nastech.com)



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