Neurocrine BIOSCIENCES

2007 ANNUAL REPORT

# A Pipeline of OPPORTUNITY

# President's Message

Kevin C. Gorman, Ph.D.
*President and Chief Executive Officer*

**DEAR SHAREHOLDERS,**

2007 was a year of challenge and change for Neurocrine, our employees, and you, our shareholders. The requirements put before us by the FDA related to indiplon were both unexpected and unforeseen. As a result of this significant obstacle, we took immediate and decisive steps to reduce our work force, refocus our priorities, and to begin reshaping the Company. It has been a difficult chapter in our history, but we now look forward to building a new Neurocrine.

As we begin 2008, I am honored to take on the role of President and CEO. In this industry changes do not happen overnight. I firmly believe that with a fresh strategy, coupled with lessons learned from the past, and a renewed strength and determination, you will see a new Neurocrine emerge. We are fortunate to have a deep and diversified pipeline, a strong financial base, and most importantly, a group of talented and committed employees. I am truly excited about the future and look forward to the challenges and opportunities that lay before us.

Our success is dependent upon three factors; advancing our current clinical pipeline into the next stages of development, research bringing additional compounds into the clinic and finally, supplementing our pipeline through external sources. Our research and development teams are focusing their skills and expertise on our three Phase II programs; gonadotropin-releasing hormone (GnRH) antagonists for endometriosis and benign prostatic hyperplasia; corticotropin-releasing factor (CRF) antagonist for anxiety, depression and irritable bowel syndrome (IBS); and Urocortin 2 for congestive heart failure.

The pipeline will be strengthened as the research group continues to advance our programs in neurologic and endocrine disorders. Additionally, our business development group is evaluating a number of products and technologies to compliment our internal efforts and grow our early stage pipeline.

**ELAGOLIX**

There are an estimated 6 million women who suffer from endometriosis. Our lead product, elagolix, an orally active GnRH antagonist, was discovered and developed by Neurocrine scientists and is currently in Phase II studies. We have completed two 3-month Phase II studies that demonstrated the ability of elagolix to lower estrogen levels and reduce pain in endometriosis patients. This was achieved without causing menopausal symptoms, apparent adverse effects on bone metabolism, or other side effects associated with current treatments for endometriosis.

In addition to these completed studies, we have three ongoing Phase IIb clinical trials with elagolix. We recently completed enrollment in the first of these studies in which 252 patients with endometriosis will be treated over a 6-month period. This study will evaluate the effect of elagolix on bone mineral density through DXA scan (X-Ray) as well as assess the impact of the drug on endometriosis symptoms. We're looking forward to top-line results from this study in the third quarter of 2008. The two other studies were launched in late 2007 and early 2008. One study is designed to determine the full dose range for elagolix, the other will serve as a head to head comparison against Lupron®. These studies will read out in early 2009. With these studies completed we will be in a position to meet with the FDA to agree upon a Phase III program.

**CRF**

GlaxoSmithKline (GSK) has three CRF compounds from our collaboration currently in the clinic for mood disorders and IBS. Two of these compounds are in Phase II and one is in Phase I trials. Recruiting was recently completed for a Phase II "proof of

concept" clinical trial in IBS with compound 876008. This study will evaluate safety and efficacy in approximately 130 patients who have met the established diagnostic criteria for IBS. We anticipate data results from this study in the second half of 2008. In early 2008, we received top-line results from 876008 in a social anxiety trial. This trial showed that there was no statistical difference between 876008 and placebo in social anxiety.

Despite this finding with 876008, we and GSK are rapidly advancing our second CRF lead compound 561679 (which is a distinct structural class from 867008) and plan to start a large Phase II trial in depression in 2008. The third CRF compound in the clinic, 586529, initiated a single escalating dose trial in early 2008.

We are excited about the progress that our CRF program is making, and have increased this program's probability of success through the clinical data that we have gathered and by having three distinct compounds in the clinic.

## UROCORTIN 2

Our Urocortin 2 program has shown encouraging efficacy and safety in the clinical setting, but we have been delayed in the preclinical setting. We have successfully dosed patients for up to four hours of continuous i.v. infusion, but prior to moving into longer durations of infusion we must complete longer-term preclinical studies. We were challenged with developing a preclinical formulation that gave high enough exposure in *in vivo* models, but we believe that we have solved this problem and are now working on completing the preclinical program in 2008. This effort will essentially conclude all of the preclinical tasks required by the FDA.

## RESEARCH

The streamlined interface between biology, chemistry and preclinical development has allowed us to more efficiently select drug targets, validate the underlying mechanism and rapidly generate lead compounds to establish *in vivo* proof of concept, including safety and pharmacokinetic profiling. Our research team is working on a number of novel neuroendocrine targets ranging from insulin regulation to neuropathic pain. The goal of the research and development group is to effectively move these programs through preclinical development and into proof of concept studies in the clinic.

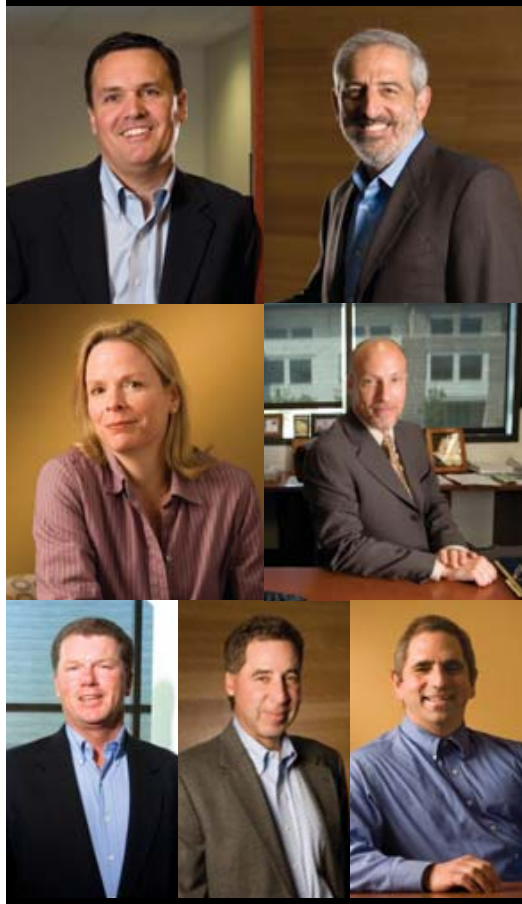
## FINANCIAL PERSPECTIVE

From a financial perspective Neurocrine remains strong; we ended 2007 with approximately $180 million in cash, essentially the same amount of funds that we started 2007. This was accomplished primarily through a controlled burn and the sale-leaseback of our corporate head-quarters. We will be managing our funds carefully while we move our clinical programs forward.

We've weathered adversity, change, and challenges and now we are moving forward and are committed to creating a new and stronger Neurocrine.

We thank our employees, collaborators and shareholders for their continued trust and support.

Kevin C. Gorman, Ph.D.
President and Chief Executive Officer



From top to bottom: Timothy P. Coughlin, CPA, *Vice President and Chief Financial Officer*; Dimitri E. Grigoriadis, Ph.D., *Vice President of Research*; Margaret E. Valeur-Jensen, Ph.D., J.D., *Executive Vice President, General Counsel and Corporate Secretary*; Christopher F. O'Brien, M.D., *Chief Medical Officer*; Hernand W. Wilson, *Vice President of Information Technology*; Richard J. Ranieri, *Senior Vice President and Chief Administrative Officer*; Haig Bozigian, Ph.D., *Senior Vice President of Pharmaceutical and Preclinical Development*

# Clinical Program Update

**NEUROCRINE'S CLINICAL DEVELOPMENT TEAM FOCUSES ON PRODUCT DEVELOPMENT IN HIGH POTENTIAL AND HIGH VALUE MARKETS WITH UNDER-SERVED MEDICAL NEEDS.**
Our clinical development team consists of Medical Doctors, Clinical Management, Clinical Research Associates, Biostatisticians, and Project Managers. They are responsible for all of our programs in various stages of clinical development.

### ELAGOLIX- GONADATROPIN-RELEASING HORMONE (GnRH) ANTAGONIST

Our orally active small molecule GnRH antagonist for endometriosis has completed 12 Phase I studies, and two exploratory Phase IIa trials. The studies have shown that elagolix is generally safe, well tolerated and has shown a reduction in the pain associated with endometriosis. Based on these results, we entered into three Phase IIb trials to further evaluate elagolix. The trials are designed to assess pelvic pain reduction offered by elagolix as well as the impact of longer term treatment of elagolix on bone mineral density. These three trials are currently underway and data will be available beginning in Q3 2008.

### CORTICOTROPIN RELEASING FACTOR (CRF) RECEPTOR ANTAGONIST

We are developing CRF receptor antagonists for depression and stress related disorders to provide a novel mechanism of action that we believe offers the advantage of being more effective than currently available therapies. We have a strategic position in the CRF field through our intellectual property portfolio and extensive knowledge of the CRF system. Since our CRF program was partnered with GSK in 2001, this collaboration has generated three promising compounds with distinct chemical characteristics that are currently in clinical development. The first compound, 876008, is in a Phase II IBS study that is fully enrolled. The second CRF compound, 561679, will enter a Phase II depression study during 2008. The third compound in the CRF program, 586529, has recently started a Phase I single escalating dose study.

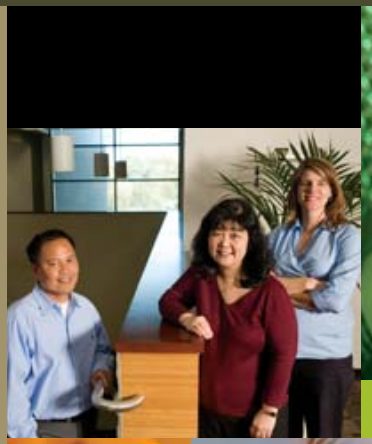
### UROCORTIN 2 (CRF-2 RECEPTOR PEPTIDE AGONIST)

Congestive Heart Failure (CHF) is a condition that requires over one million hospitalizations a year in the United States. We have capitalized on our extensive CRF knowledge to develop our Urocortin 2 program. We have completed several clinical trials in patients and these trials demonstrated that our drug candidate was generally well tolerated with positive hemodynamic effects and increases in cardiac output without serious adverse events. Preclinical studies are currently being completed to support a longer infusion period (up to 72 hours) for the next segment of clinical trials.

### GnRH-BENIGN PROSTATIC HYPERPLASIA (BPH)

BPH is characterized by the enlargement in the prostate gland where the prostate growth impinges on the urethra. Researchers have determined that dihydrotestosterone (DHT), a derivative of testosterone, is the primary cause of prostate enlargement. We completed a Phase I study and the results of this two week dosing study demonstrated that a dose related reduction of testosterone was achieved and was generally safe and well tolerated.

**The Neurocrine Spirit** Through challenge comes opportunity, through adversity comes strength, and through change comes new thinking. The team environment at Neurocrine was tested this year, yet the Neurocrine spirit continues to shine as our employees embrace the change and refocus their efforts to bring our four Phase II drug candidates and our other clinical and research compounds forward. We believe our experience and spirit will help us to continue to develop novel therapies that will benefit patients worldwide and build shareholder value in the years to come.









# PRODUCT PIPELINE

## Products Under Development

| | | |
|---|---|---|
| **Elagolix** | **Indication:** Endometriosis<br>**Commercial Rights:** Neurocrine |  Orally active small molecule |
| **GnRH Antagonist** | **Indication:** Benign Prostatic Hyperplasia<br>**Commercial Rights:** Neurocrine |  21 million BPH sufferers in the US  |
| **$CRF_1$ Antagonist (561679)** | **Indication:** Anxiety/Depression<br>**Commercial Rights:** Neurocrine/GlaxoSmithKline |  Partnered with GlaxoSmithKline |
| **$CRF_1$ Antagonist (876008)** | **Indication:** Irritable Bowel Syndrome (IBS)<br>**Commercial Rights:** Neurocrine/GlaxoSmithKline |  Partnered with GlaxoSmithKline |
| **$CRF_1$ Antagonist (586529)** | **Indication:** Anxiety/Depression<br>**Commercial Rights:** Neurocrine/GlaxoSmithKline |  Partnered with GlaxoSmithKline |
| **$CRF_2$ Peptide Agonist (Urocortin 2)** | **Indication:** Cardiovascular<br>**Commercial Rights:** Neurocrine |  5 million people with congestive heart failure (CHF) in US |

## Research Programs

| | | |
|---|---|---|
| sNRI | **Indication:** Neuropathic Pain | **Commercial Rights:** Neurocrine |
| Glucose Dependent Insulin Secretagogues | **Indication:** Type II Diabetes | **Commercial Rights:** Neurocrine |
| GnRH Antagonist | **Indication:** Women's and Men's Health | **Commercial Rights:** Neurocrine |
| Ion Channel Blocker | **Indication:** Chronic Pain | **Commercial Rights:** Neurocrine |

## Indiplon

| | | | |
|---|---|---|---|
| 5mg and 10mg capsules | **Indication:** Insomnia | **Commercial Rights:** Neurocrine/Dainippon Sumitomo Pharma Co. (Japan) | FDA approvable letter received December 12, 2007. |
| 15mg tablets | **Indication:** Insomnia | **Commercial Rights:** Neurocrine | FDA not-approvable letter received May 15, 2006. |

# RESEARCH

"Research" indicates identification and evaluation of compound(s) in laboratory and preclinical models.

## PHASE 1

70 million women worldwide are stricken with endometriosis
1 in 10 women in the US suffer from endometriosis

40% of men over the age of 60 suffer from symptoms of BPH

US has 20 million major depressive disorder sufferers

22-45 million people in the US suffer
from gastrointestinal disorders

US has 20 million anxiety sufferers

660,000 new CHF cases each year

## PHASE 2

Costs of endometriosis in US = $20 billion

121 million sufferers worldwide

Costs of IBS in US = $25 billion

Costs of CHF in US = $35 billion

**Neurocrine's Research team has expertise in identifying small molecule clinical candidates aimed at GPCRs, transporters and ion channels. Our in-depth understanding of the underlying mechanisms involved in ligand/protein interactions offers us a unique and opportunistic advantage with a variety of protein targets involved in multiple disease states. This effort has translated into identifying new chemical entities with distinct pharmacological profiles that demonstrate proof of concept in *in vivo* models of disease, allowing us to advance into preclinical testing and clinical trials with these distinct molecules. In addition to utilizing this technology in our existing later stage programs, we are applying this knowledge to novel targets within our portfolio. With the goal of delivering one new drug candidate into the clinic every 12 months, the Research group continues to advance novel small molecule compounds into development focusing on diseases and disorders of the central nervous and endocrine systems.**

## PHASE 3

"Phase 1" indicates that clinical trials are being conducted with a smaller number of subjects to determine early safety profile, maximally tolerated dose and pharmacological properties of the compound.

"Phase 2" indicates that clinical trials are being conducted on groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.

"Phase 3" indicates that large-scale clinical trials are being completed to provide primary support for FDA approval.

# Corporate Information

## CORPORATE MANAGEMENT

Kevin C. Gorman, Ph.D.
*President and Chief Executive Officer*

Margaret E. Valeur-Jensen, Ph.D., J.D.
*Executive Vice President, General Counsel and Corporate Secretary*

Richard J. Ranieri
*Senior Vice President and Chief Administrative Officer*

Timothy P. Coughlin, CPA
*Vice President and Chief Financial Officer*

Christopher F. O'Brien, M.D.
*Chief Medical Officer*

Haig Bozigian, Ph.D.
*Senior Vice President of Pharmaceutical and Preclinical Development*

Dimitri E. Grigoriadis, Ph.D.
*Vice President of Research*

Hernand W. Wilson
*Vice President of Information Technology*

## BOARD OF DIRECTORS

Joseph A. Mollica, Ph.D.
*Chairman of the Board, Neurocrine Biosciences, Inc. and Chairman of the Board, Pharmacopeia Inc.*

Gary A. Lyons
*Former President and Chief Executive Officer, Neurocrine Biosciences, Inc.*

Kevin C. Gorman, Ph.D.
*President and Chief Executive Officer, Neurocrine Biosciences, Inc.*

Corinne Lyle
*President, Global Operations, Edwards Lifesciences Corporation*

W. Thomas Mitchell
*Former Chairman of the Board and Chief Executive Officer of Genencor International*

Richard F. Pops
*Chairman of the Board, Alkermes, Inc.*

Stephen A. Sherwin, M.D.
*Chairman of the Board and Chief Executive Officer, Cell Genesys, Inc.*

Wylie W. Vale, Ph.D.
*Professor & Head, The Clayton Foundation Laboratories for Peptide Biology The Salk Institute*

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## CORPORATE HEADQUARTERS

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Fax: (858) 617-7602
www.neurocrine.com

## AUDITORS

Ernst & Young LLP

## TRANSFER AGENT

American Stock Transfer

## SEC FORM 10-K

A copy of the Company's annual report to the Securities and Exchange Commission on Form 10-K is available without charge, upon written request to:

Neurocrine Biosciences, Inc.
12790 El Camino Real
San Diego, CA 92130

## SAFE HARBOR STATEMENT

Any statements in this report about our expectations, beliefs, plans, objectives, assumptions or future events or performance that are not historical facts are forward-looking statements. You can identify these forward-looking statements by the use of words or phrases such as "believe," "may," "could," "will," "estimate," "continue," "anticipate," "intend," "seek," "plan," "expect," "should" or "would." Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation, statements about our ability to create market demand for and generate revenues from our products; unexpected adverse side effects or inadequate therapeutic efficacy of our products that could delay or prevent product development or commercialization, or that could result in product recalls or product liability claims; the scope and validity of patent protection for our products and our ability to commercialize our products without infringing the patent rights of others; competition from other pharmaceutical or biotechnology companies; the progress and timing of our clinical trials; other difficulties or delays in development, testing, obtaining regulatory approvals, manufacturing and marketing of our products; our ability to obtain additional financing to support our operations; and other risks detailed in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2007, which accompanies this report.

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.