### ACADIA PHARMACEUTICALS 2014 ANNUAL REPORT→



## ABOUT US

We are a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in neurological and related central nervous system disorders. We have a pipeline of product candidates led by NUPLAZID™ (pimavanserin), which has successfully completed Phase III development and has the potential to be the first drug approved in the United States for Parkinson's disease psychosis. We also are developing pimavanserin in additional areas with severe unmet medical needs, including Alzheimer's disease psychosis and schizophrenia.



#### STEPHEN R. DAVIS

INTERIM CHIEF EXECUTIVE OFFICER

## What is the biggest opportunity for ACADIA Pharmaceuticals?

Our pipeline of product candidates is led by NUPLAZID™ (pimavanserin), which offers a new and distinctly different pharmacological approach to treating psychosis. We believe this next-generation approach holds the potential to dramatically change the way we think about treating psychosis - offering relief without many of the compromises inherent in existing therapies. We have completed our Phase III program to develop NUPLAZID for Parkinson's disease psychosis (PDP) and expect to submit our New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) in the second half of 2015.

NUPLAZID has the potential to be the first drug approved in the United States for the treatment of psychosis associated with Parkinson's disease. We also are developing pimavanserin for Alzheimer's disease psychosis and schizophrenia – other areas with severe unmet medical needs. In addition, we have collaborative clinical-stage programs for chronic pain and glaucoma.

#### What is ACADIA's strategic vision?

At ACADIA, our strategy remains unchanged. Our vision is to become a leading biopharmaceutical company dedicated to developing and commercializing innovative therapies for neurological and related central nervous system (CNS) disorders. We are excited about the opportunity to build a U.S. specialty CNS franchise using pimavanserin as the foundation. We see a broad opportunity for pimavanserin to expand into a range of neurological and psychiatric indications and the potential to transform



the treatment paradigm in large underserved disease states

# What progress did ACADIA make in 2014?

Last year we made important progress in advancing NUPLAZID toward registration. We successfully completed our drug-drug interaction program and our stability program for registration batches and held successful pre-NDA meetings with the FDA. We also continued to make significant strides in our commercial preparations for the planned launch of NUPLAZID in the United States.

In addition, the FDA designated
NUPLAZID as a Breakthrough Therapy, which
reinforces the serious unmet medical need
in PDP and the importance of our NUPLAZID
program. We are pleased NUPLAZID met the
criteria for the Breakthrough Therapy
designation, which the FDA created to
expedite the development and review of
drugs that are intended to treat serious or
life-threatening conditions.

# For ACADIA, what are the most important priorities going forward?

Our highest priority is the planned submission of our NUPLAZID NDA. To that end, we are focused on preparing the organization for the submission and review of the NDA and the planned U.S. launch of NUPLAZID. In addition, we continue expanding our medical and development capabilities to further leverage pimavanserin and its lifecycle opportunities.

## What are the next steps in the NDA submission of NUPLAZID for PDP?

Moving from a clinical-stage company to a commercial-stage company requires building infrastructure to accommodate commercial-scale operations. As we announced in March 2015, additional time was needed to complete the preparation of manufacturing quality systems to support commercial manufacturing and supply. We are focused on ensuring that we have established, tested and evaluated the appropriate manufacturing and supply



## BY THE NUMBERS

PARKINSON'S DISEASE PSYCHOSIS (PDP)

40%

PDP afflicts about 40% of the 1 million Parkinson's patients in the United States.

70%

Over 70% suffer comorbid sleep disturbances.

90%

Almost 90% have caregiver support with 74% requiring daily care.

ALZHEIMER'S DISEASE PSYCHOSIS (ADP)

25-50%

ADP afflicts about 25% to 50% of the 5.2 million Alzheimer's disease patients in the United States.

Zero

Currently there is no drug approved by the FDA for ADP.

**SCHIZOPHRENIA** 

3 Million

There are approximately 3 million people in the United States suffering from schizophrenia.

74%

In a landmark government study, about 74% of patients with schizophrenia discontinued their medications because of lack of efficacy or intolerable side effects. systems to prepare for FDA review and

## How are you preparing for commercialization?

Over the last year, our commercial team has focused on thoroughly understanding the PDP market landscape and preparing the product, the market, and the organization for commercial launch. We conducted extensive market research with neurologists, psychiatrists and long-term care clinicians as well as PDP patients and their caregivers. We conducted scientific advisory boards with leading movement disorder specialists and PDP-treating physicians in order to gain insight regarding how to position NUPLAZID to best address the needs of patients, caregivers and physicians. We completed foundational access and reimbursement research with key decision-makers for payors covering 168 million lives. We also completed important sales-force sizing assessments and preparation of commercial infrastructure and systems for launch remains on track.

In January 2015 we launched a PDP disease awareness campaign in the physician community and are conducting an extensive speaker training program to educate healthcare professionals on PDP. We also continue to build out a medical affairs organization of highly experienced professionals to support the introduction of

NUPLAZID, if approved. Our teams are energized by the potential of NUPLAZID to make a meaningful impact on the lives of patients with PDP and their caregivers.

# How do you plan to market NUPLAZID for PDP?

ACADIA owns the worldwide commercialization rights to NUPLAZID. In the United States, our senior commercial team has been building the commercial organization and advancing our commercial readiness per plan. In connection with this plan we expect to hire approximately 135 sales representatives at or around the time of approval. Our specialty sales force will be dedicated to covering the estimated 11,000 PDP-treating physicians, with the largest segment being neurologists.

In parallel with the advancement of our PDP program in the United States, we also have outlined the path to registration for NUPLAZID in Europe. During 2015, we will be working on our Marketing Authorization Application (MAA) for NUPLAZID for submission to the European Medicines Agency (EMA) approximately six to nine months following the submission of our NDA

#### What is the impact of PDP?

Parkinson's disease affects about one million people in the United States and between four to six million people globally and is the second most common

## PARKINSON'S DISEASE PSYCHOSIS (PDP)

#### LARGE UNMET NEED



"Among Parkinson's patients, psychosis causes great distress for patients and caregivers and is the leading cause of institutionalization. Neurologists have limited options to treat this serious disorder, and off-label use of current antipsychotics is linked to increased risk of death and serious adverse events, as well as loss of motor control."

- **Jeffrey Cummings**, M.D., Sc.D. Director of Cleveland Clinic , Lou Ruvo Center for Brain Health



"When we recently examined the topics that were most searched for on our National Parkinson Foundation's website, we were not surprised to discover that treatment of psychosis, comprising hallucinations and delusions, topped the list. There is a critical unmet need for development of better drugs to address psychosis in the setting of Parkinson's disease."

- **Michael S. Okun**, M.D. National Medical Director. National Parkinson Foundation



neurological disorder after Alzheimer's disease. Research indicates that at any point in time approximately 40 percent of patients with Parkinson's disease also suffer from PDP and that over a lifetime, a majority of patients with Parkinson's disease eventually develop PDP. PDP is a debilitating disorder characterized by hallucinations and delusions that worsens over time and severely impacts daily living. Research has shown that delusions often involve suspicions of spousal infidelity or other paranoid themes and are often disturbing and debilitating to patients. PDP substantially contributes to the burden of Parkinson's disease and deeply affects a patient's quality of life. PDP is also associated with increased caregiver distress and burden, nursing home placement, and increased mortality and morbidity.

What is the current treatment for PDP?

Currently, no drug is approved to treat PDP in the United States and the problem is expected to grow as our population ages.

The condition is often treated off label with atypical antipsychotics, which can worsen the symptoms of Parkinson's disease and carry a black box warning for use in elderly patients with dementia-related psychosis due to increased risk of mortality and morbidity. Physicians treating patients with PDP face a "dopamine dilemma," because drugs used to treat the psychosis can exacerbate the motor symptoms associated with Parkinson's disease.

At ACADIA, we are developing NUPLAZID as a potential first-in-class treatment for PDP. Pimavanserin – a small molecule that was discovered in our laboratories – has a unique mechanism of action as a selective serotonin inverse agonist preferentially targeting 5-HT<sub>2A</sub> receptors. Outcomes from NUPLAZID's successful Phase III clinical trial, referred to as the -020 Study, indicate that NUPLAZID has the potential to provide a safe and effective treatment of PDP without compromising motor control or causing daytime sedation.

#### **OUR PIPELINE**

COMPOUND/ PROGRAM	INDICATION	IND-TRACK	PHASE I	PHASE II	PHASE III	REGULATORY APPROVAL	COMMERCIALIZATION RIGHTS
NUPLAZID™ (pimavanserin)	Parkinson's Disease Psychosis			:			ACADIA
	Alzheimer's Disease Psychosis			<b>-</b>			
	Schizophrenia			<b>-</b>			
Adrenergic	Chronic Pain						Allergan
Muscarinic	Glaucoma						Allergan

# What is the opportunity to develop pimavanserin for Alzheimer's disease psychosis?

We believe pimavanserin has the potential to establish a new paradigm in the way psychosis is treated and we plan to explore pimavanserin in multiple indications. Currently, in addition to our plans to seek approval of pimavanserin in PDP, we are conducting a Phase II study of pimavanserin in Alzheimer's disease psychosis (ADP) and expect to complete enrollment by the end of 2015.

Like PDP, no drug is currently approved in the United States for the treatment of ADP. Atypical antipsychotics are frequently used off label to treat ADP despite the black box warnings of increased risk of mortality and morbidity in this patient population. In addition, research indicates that the use of atypical antipsychotics in ADP patients worsens their cognitive deficits in a manner equivalent to approximately one year's disease progression.

According to the Alzheimer's
Association, an estimated 5.2 million
people in the United States have
Alzheimer's disease. Studies have
suggested that approximately 25 percent
to 50 percent of Alzheimer's patients may
develop psychosis, commonly consisting
of hallucinations and delusions. The
psychosis in Alzheimer's patients is
associated with even more rapid cognitive
and functional decline and increased
institutionalization relative to Alzheimer's
patients without psychosis.

# What other indications are currently planned for the development of pimavanserin?

We are planning a Phase II clinical study with pimavanserin as a mono-therapy treatment for the maintenance phase of schizophrenia – that is, the period of time between acute psychotic episodes. We believe the pimavanserin profile may allow for an improved schizophrenia therapy resulting in better compliance and safety



compared to existing antipsychotic drugs.
Schizophrenia is a debilitating lifelong
disease afflicting approximately 1 percent of
the population globally, and current
therapies are suboptimal.

We are also planning to initiate a
Phase II study to further explore the
potential sleep benefits of pimavanserin in
Parkinson's disease patients. In clinical
studies we observed non-sedating sleeprelated benefits of pimavanserin, including
a significant improvement in both nighttime
sleep and daytime wakefulness compared
to placebo. Sleep disorders are a major and
frequent problem for patients with
neurological disorders, and studies
suggest that nighttime sleep disturbances
occur in around 70 percent of Parkinson's
disease patients.

#### What is ACADIA's financial position?

We remain in a strong financial position to launch NUPLAZID for PDP and also to explore other areas where pimavanserin may have a profound impact in the treatment of other disorders. We strengthened our balance sheet in 2014, raising \$197 million in net proceeds from

our public offering of common stock and closing the year with \$322.5 million in cash and cash equivalents. We believe our cash runway positions us to continue making the kinds of investments that we believe will leverage the full potential of pimavanserin.

# How can ACADIA help improve the lives of patients and caregivers?

At ACADIA, we are developing innovative therapies that can improve the lives of patients and the family members who care for them every day. This passion is what drives everything we do at ACADIA. I want to acknowledge our team for their hard work, commitment and expertise. In the last year, we have brought in highly qualified individuals with extensive experience in their functional domain and in CNS products. I look forward to updating you on our progress as we build ACADIA into a leading biopharmaceutical company with significant promise in the CNS area.

**Stephen R. Davis**Interim Chief Executive Officer
April 2015

#### Uli Hacksell, Ph.D.

After 16 years of service, Uli Hacksell, Ph.D. retired in March 2015. Under Uli's leadership as CEO, ACADIA grew from a small startup to a fast-growing biopharmaceutical company with innovative drug candidates. We thank him for his contributions to the Company. His dedication, tenacity, deep knowledge of the CNS space, and life-long passion to deliver new drugs that can improve the lives of patients with CNS disorders have benefited ACADIA greatly. We wish Uli all the best in his retirement.

#### EXECUTIVE OFFICERS

#### Stephen R. Davis

Interim Chief Executive Officer

#### Roger G. Mills, M.D.

Executive Vice President,
Development and Chief Medical Officer

#### Terrence O. Moore

Executive Vice President and Chief Commercial Officer

#### Glenn F. Baity

Executive Vice President, General Counsel and Secretary

#### BOARD OF DIRECTORS

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#### Daniel B. Soland

Former Senior Vice President and Chief Operating Officer, ViroPharma

#### William (Bill) M. Wells

Founder and Chairman, Evizone Limited Former Chief Executive Officer Biovail Corporation

#### CORPORATE HEADQUARTERS

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#### COMMON STOCK LISTING

Ticker Symbol: ACAD, The NASDAQ Global Select Market

#### ANNUAL STOCKHOLDERS' MEETING

ACADIA Pharmaceuticals' Annual Stockholders' Meeting will be held on Monday, June 15, 2015, at the offices of Cooley LLP, 4401 Eastgate Mall, San Diego, CA 92121.

## STOCK TRANSFER AGENT AND REGISTRAR

Computershare Trust Company, N.A. 250 Royall St. Canton, MA 02021 Telephone: (800) 851-3061 www.computershare.com/us

### INDEPENDENT REGISTERED PUBLIC

Ernst & Young LLP

#### STOCKHOLDERS' INQUIRIES

Stockholders may obtain copies of our news releases, Securities and Exchange Commission filings, including Forms 10-K, 10-Q, and 8-K, and other company information by accessing our website at www.acadia-pharm.com. Stockholders may also contact Investor Relations at (858) 558-2871.

#### FORWARD-LOOKING STATEMENTS

Statements in this report that are not strictly historical in nature are forward-looking statements. These statements include but are not limited to statements related to the progress and timing of our drug development programs and related trials and regulatory filings, the utility, safety, efficacy and benefits of our product candidates, the future development and commercialization of pimavanserin in a variety of indications, potential approval of NUPLAZID™ (pimavanserin), opportunities and potential for pimavanserin, and future growth for ACADIA or its stockholders. These statements are only predictions representing ACADIA's expectations and beliefs as of the date this report was prepared based on then-current information. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in drug discovery, development and commercialization, risks associated with regulatory review and approval, and the risk that past results of clinical trials may not be indicative of future trial results. For a discussion of these and other factors, please refer to ACADIA's Annual Report on Form 10-K for the year ended December 31, 2014, as well as other subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All forward-looking statements are qualified in their entirety by this cautionary statement and ACADIA undertakes no obligation to revise or update this report to reflect future events or circumstances after the date hereof, except as required by law.



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