ANNOVIS

Attacks Alzheimer's Disease and Neurodegeneration by Improving the Information Highway of the Nerve Cell

Axonal Transport

Symbol: **ANVS** (NYSE American)

June 2020

FORWARD-LOOKING STATEMENTS

Statements in this presentation contain "forward-looking statements" that are subject to substantial risks and uncertainties. Forward-looking statements contained in this presentation may be identified by the use of words such as "anticipate," "expect," "believe," "will," "may," "should," "estimate," "project," "outlook," "forecast" or other similar words, and include, without limitation, statements regarding Annovis Bio, Inc.'s expectations regarding the trading of its shares on the NYSE American market. Forward-looking statements are based on Annovis Bio, Inc.'s current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in the Annual Report on Form 10-K for the year ended December 31, 2019 filed with the Securities and Exchange Commission. Forward-looking statements contained in this presentation are made as of this date, and Annovis Bio, Inc. undertakes no duty to update such information except as required under applicable law.

HIGHLIGHTS

A novel approach to treat neurodegeneration is desperately needed

- **Annovis is developing drugs** for Alzheimer's (AD) and Parkinson's disease (PD), including the orphan indication Alzheimer's in Down Syndrome (AD-DS)

- **Lead compound, ANVS401,** is the only drug to improve axonal transport, the information highway of the nerve cell, by attacking multiple neurotoxic proteins
- **Two phase 2a studies**
  - AD trial already underway
  - PD trial to be initiated
- **Successful completion of the two phase 2a** will allow start of two phase 3 studies
- **Highly experienced and respected management team, great board and world renowned scientific advisory board**

THE STATE OF ALZHEIMER'S DISEASE

- Alzheimer's is the most common cause of dementia, a general term for memory loss and other cognitive abilities serious enough to interfere with daily life. **Alzheimer's disease accounts for 60 to 80 percent of dementia cases.**
- **1 in 6 females and 1 in 11 males** have the chance to develop Alzheimer's during the remainder of their lives at age 65.
- **From 1998 to 2018 there have been over 500 failed attempts at developing Alzheimer's drugs.**
- **The sector needs to rethink dementia**, develop new approaches and create new drugs.

ALZHEIMER'S DRUG TRIAL FAILURES

Have researchers been on the wrong track with amyloid?

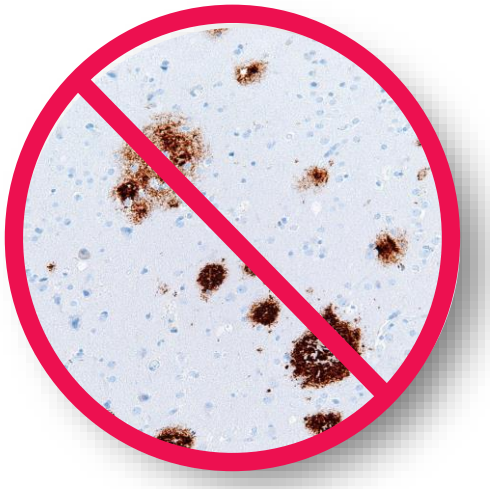
STAT+

> *The idea that sticky brain plaques cause Alzheimer's disease began as an interesting hypothesis and eventually became drug industry dogma. Now, after a string of clinical trial failures, that hypothesis looks less credible than ever. But how did nearly two decades of failure not convince the brightest minds in pharma that it was time to move on?*
>
> Damian Garde & Alex Hogan

Amyloid Plaque and Aβ is NOT The Only Answer

After amyloid failures, it's time to take a new tack for treating Alzheimer's

Raymond J. Tesi STAT News April 30, 2019



Aducanumab's failure puts pressure on field to look beyond amyloid

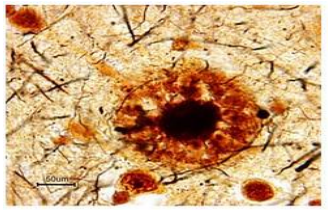
Ned Pagliarulo March 22, 2019

ANNOVIS' DRUG TREATS AD AND PD

Chronic and acute brain insults lead to high levels of neurotoxic proteins, to inflammation and neurodegeneration

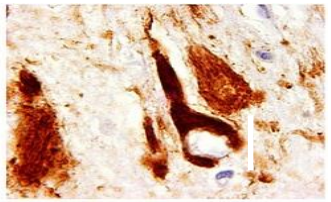
Amyloid β

AD / PD- Aβ Targeting Compounds



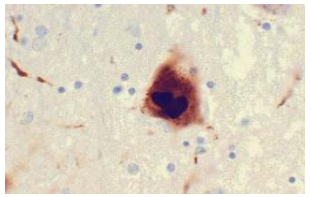
Tau

Tauopathies - AD - Tau Targeting Compounds

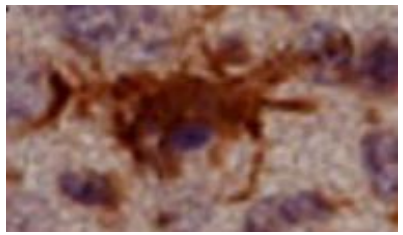


aSynuclein

PD / AD - aSYN Targeting Compounds



ACTIVATED MICROGLIA = *High Inflammation*

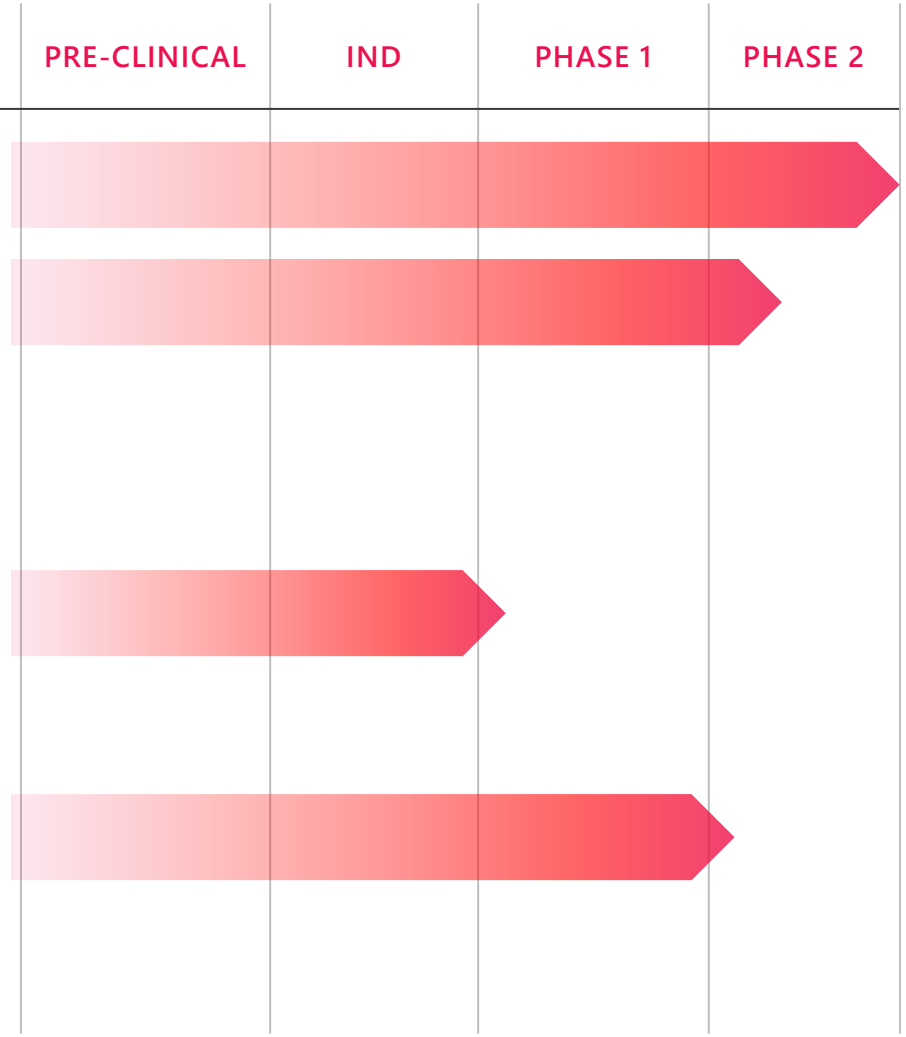


Attacking one neurotoxic protein results in minimal effect

ANVS401 is the only drug to attack multiple neurotoxic proteins simultaneously

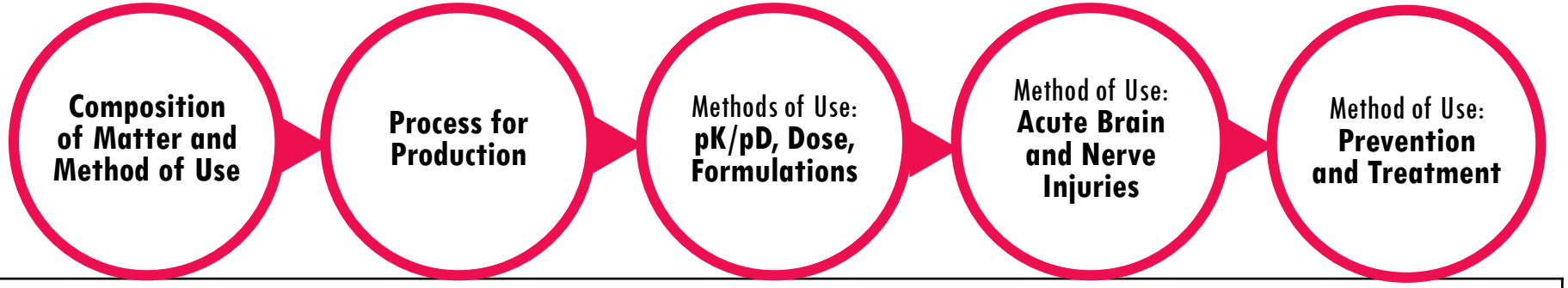
PIPELINE

	DISEASE	NEUROTOXIC PROTEIN TARGET
ANVS401 Oral drug for chronic indications	AD (AD-DS)	APP, tau, aSYN
	PD	aSYN, APP
ANVS405 injectable drug for acute traumatic events	TBI	Tau, APP, aSYN
ANVS301 oral drug for advanced AD and dementia	Advanced AD	BChEI



CORPORATE PATENT ESTATE

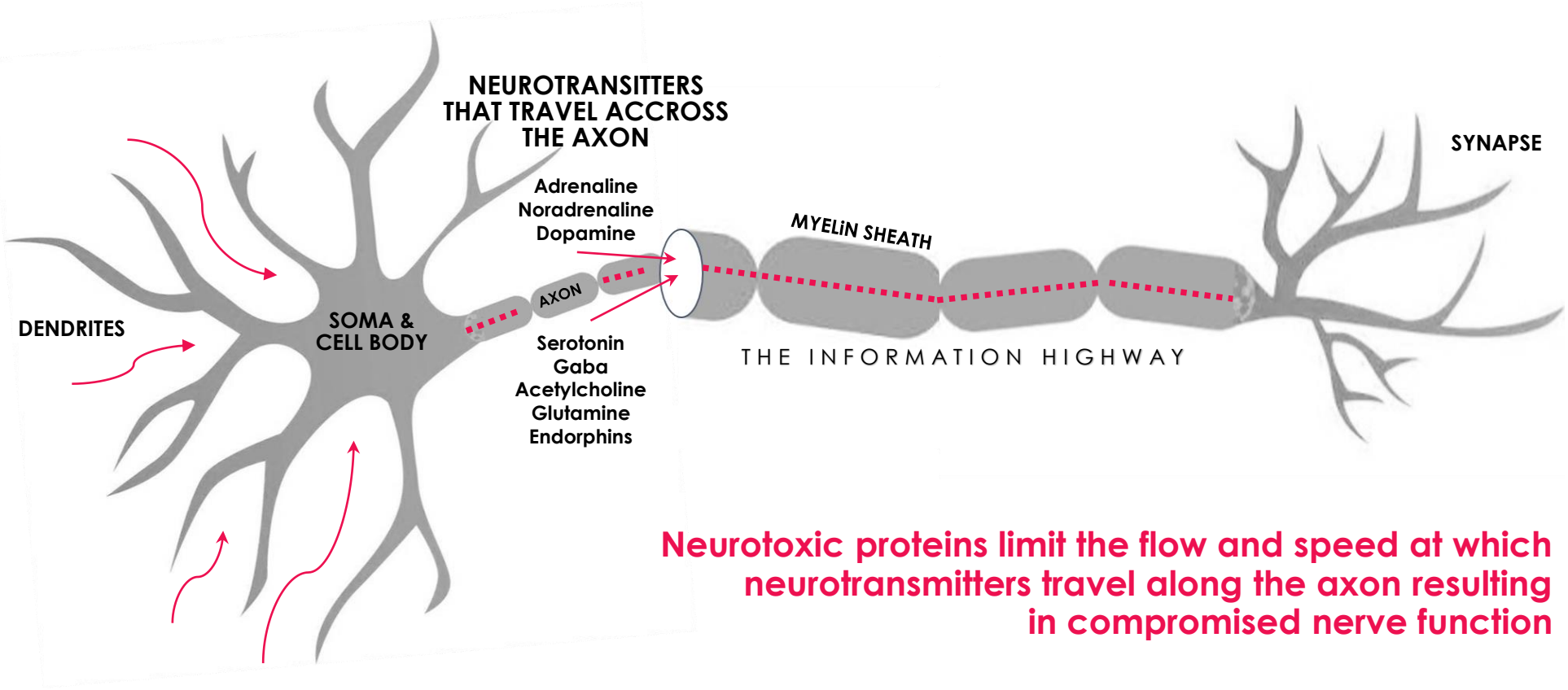
Multi-layer strategy



Patent/Application	Subject Matter	Status US	Expiry US
Provisional	ANVS401 to treat viral and bacterial infections of the brain, including Covid19	Pending	**2041**
PCT	ANVS401 and 405 - Method of use of MOA for prevention and treatment of diseases	Pending	**2038**
PCT	ANVS405 - Acute brain and nerve injuries	Pending	**2036**
PCT	ANVS401 - pK/pD, low doses, formulations Neurodegenerative Diseases	**US 10,383,851; 07-2019 EP 2683242; 03-2020**	**2031**
In-licensed patents	Composition of matter, manufacturing, method for treating AD and DS	Granted	**2022-25**

HOW NERVE CELLS WORK

In healthy nerve cells little packages containing neurotransmitters or nerve growth factors travel unimpaired from the cell body through the axon to the synapse.



Neurotoxic proteins limit the flow and speed at which neurotransmitters travel along the axon resulting in compromised nerve function

NEUROTOXIC PROTEINS IMPAIR AXONAL TRANSPORT AND **CAUSE A TOXIC CASCADE**

HIGH LEVELS OF NEUROTOXIC PROTEINS

- IMPAIRED AXONAL TRANSPORT
- SLOWER SYNAPTIC TRANSMISSION
- INFLAMMATION
- DEATH OF NERVE CELLS
- LOSS OF COGNITIVE AND MOTOR FUNCTION

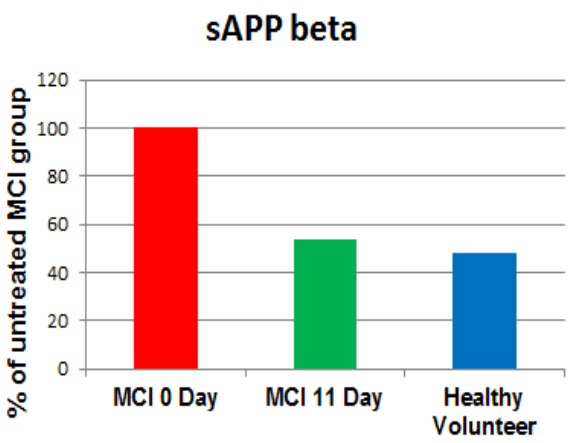
ANVS401 LOWERS LEVELS OF NEUROTOXIC PROTEINS

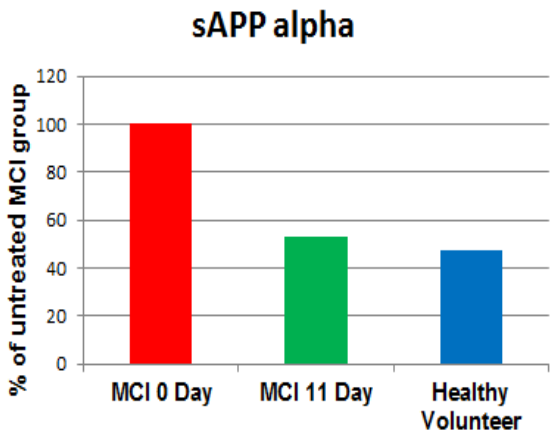
- IMPROVED AXONAL TRANSPORT
- INCREASED SYNAPTIC TRANSMISSION
- NO INFLAMMATION
- HEALTHY NERVE CELLS
- IMPROVED COGNITIVE AND MOTOR FUNCTION

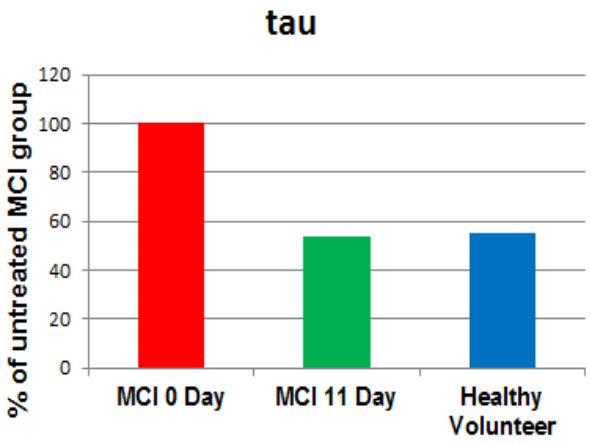
ANVS401 IMPROVES AXONAL TRANSPORT AND **IMPEDES THE TOXIC CASCADE**

RESULTS IN HUMANS

ANVS401 Lowers Neurotoxic Proteins in Spinal Fluid of MCI Patients







Maccecchini et al: JNNP 2012; 83: 894-902

- In this proof of concept study, ANVS401 lowers the levels of APP/Aβ, tau/p-tau and aSYN back to the levels seen in healthy volunteers
- It lowers the levels of the three neurotoxic proteins causing AD and PD

NEURODEGENERATION IS AN AXONAL TRANSPORT DISEASE

Axonal transport is responsible for:

- Neurotransmitters GABA (anxiety), ACh (cognition), dopamine (movement), serotonin (mood)
- Neurotrophic factors NGF, BDNF
- All communication within and between nerve cells

> Newly published Nature Review Article (September 2019):
>
> *"Axonal transport disruption is linked to human neurological conditions."*

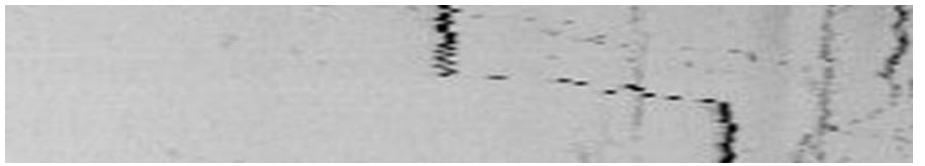
Retrograde (0.5 frame/sec)

Normal Transport

The ***Normal Flow and Speed*** of vesicles carrying BDNF across the axon.

Abnormal Transport

Shows the ***Blockage and Slowing*** of BDNF across the axon. Black areas demonstrate where transport is slowed due to high levels of neurotoxic proteins.



TREATED WITH ANVS401

The ***Flow and Speed*** of axonal transport is improved.

APP, Ab42, C99 – Mobley, UCSD; aSYN – Isacson, Harvard; Lee, U.Penn;
Tau – U. Muenich & Zuerich; Htt – Mobley, UCSD; TDP43 – Taylor, Northwestern

ANVS401 LOWERS INFLAMMATORY MARKERS

CSF Inflammatory Markers Significantly Decrease After 10 Days of Oral ANVS401 in MCI Patients

Inflammatory Protein	CSF % of Baseline	p-Value
Complement C3	-86.9%	0.0007
MCP-1	-87.5%	0.0007
YKL40	-72.7%	0.0113
sCD14	-26.1%	0.1159
Factor FH*	23.7%	0.4988

* Control Factor

Maccecchini et al: JNNP 2012; 83: 894-902

RESULTS IN ANIMALS

19 animal studies showed that ANVS401 and ANVS405 improved the affected function

ANVS401

ANVS405

- ✓ **ANVS401 and ANVS405 increased memory and learning in three animal models:**
  - AD tg mice
  - DS trisomic mice
  - TBI rats

ANVS401

- ✓ **Improved gut motility** in PD tg mice
- ✓ **Stabilized brain chemistry** in FTD tau tg mice

ANVS405

- ✓ **Protected retinal cells** in acute glaucoma in rats

TWO PHASE 2 CLINICAL TRIALS IN AD AND PD

TRIALS

1) AD with 24 patients for one month
   - ongoing (14 patients treated)

2) PD and AD with 68 patients for one month
   - to start in June

ENDPOINTS

Target Engagement

Decrease in neurotoxic protein levels

Pathway Engagement

Increase in neurotransmitters and neurotrophic factors

Lowering of inflammatory proteins

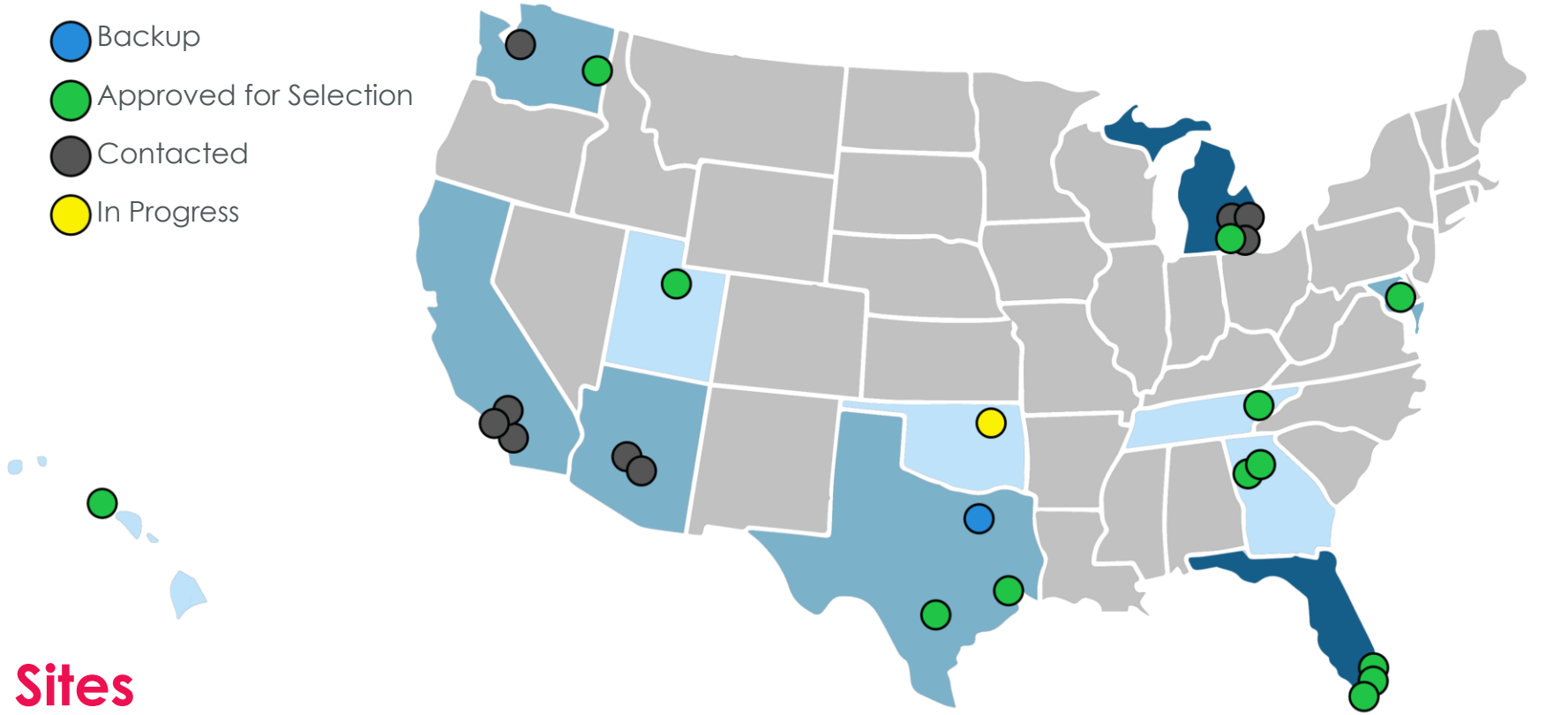
Lowering of neurodegeneration markers

Cognitive Outcomes and Functional Outcomes

CLINICAL – OVERVIEW

CRO	Parexel
Therapeutic Area	Early Alzheimer's and Parkinson's Diseases
Phase	2
Design	Double-Blind, Placebo-Controlled, 2-Cohort Biomarker Study
Country	United States
Sites	Up to 15 Sites
Patients	68 Part 1 - Comparison of 14 AD vs 14 PD Patients Part 2 - Dose Response in 40 PD Patients

CLINICAL – SITE UPDATE



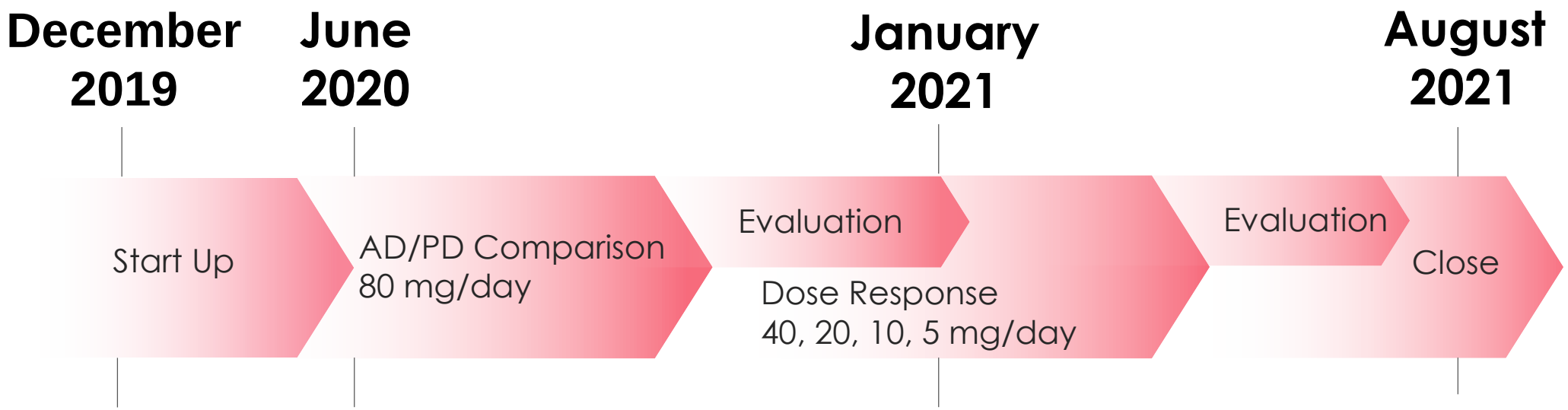
15 Sites

With Additional Back-Up Sites

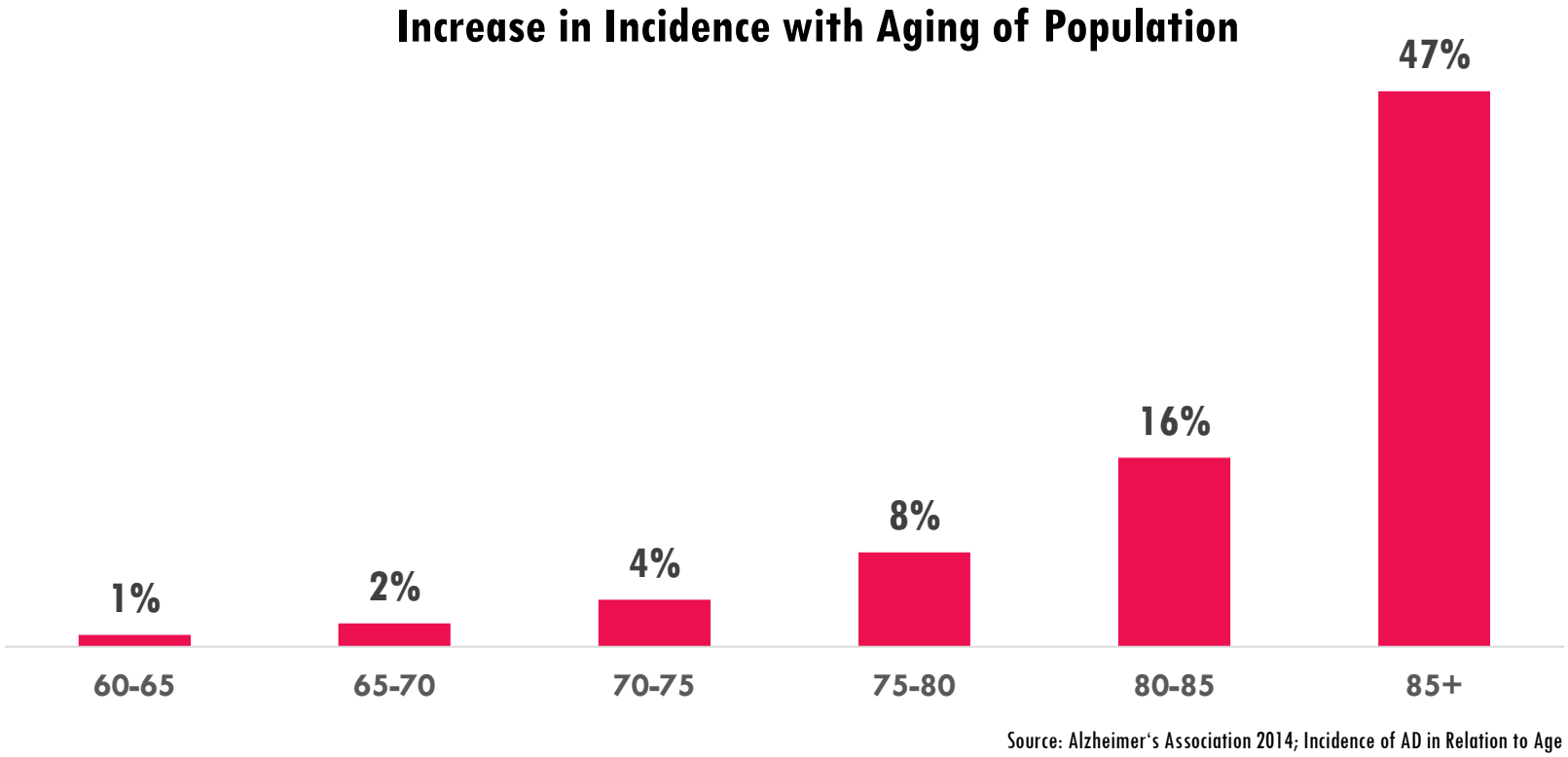
CLINICAL - TIMELINES

The two-part clinical study is being set up at 15 sites in the US and will begin in June 2020. The AD/PD comparison is projected to be concluded by the end of the year and preliminary data will be available in early 1Q2021

The dose response is projected to be completed by mid summer next year



MARKET PROJECTIONS



Source: Alzheimer's Association 2014; Incidence of AD in Relation to Age

Annual sales potential for US and worldwide are over $100 billion dollars

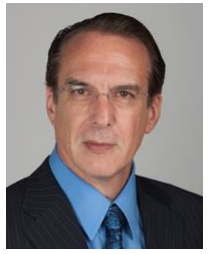
CHIEF EXECUTIVES AND CHIEF ADVISORS

Maria L. Maccecchini, PhD Founder, President & CEO

Founded Annovis in May 2008 to develop better therapeutics for Alzheimer's, Parkinson's and other neurodegenerative diseases. Was partner and director of two angel groups, Robin Hood Ventures and MidAtlantic Angel Group; Founder and CEO of Symphony Pharmaceuticals/Annovis a biotech company that sold in 2001 to Transgenomic; General Manager of Bachem Bioscience, the US subsidiary of Bachem AG, Switzerland and Head Molecular Biology Mallinckrodt; Dr. Maccecchini did one postdoc at Caltech and one at the Roche Institute of Immunology, her PhD in biochemistry is from the Biocenter of Basel with a two-year visiting fellowship at The Rockefeller University.

Jeffrey McGroarty, CPA, MBA, Chief Financial Officer

Jeff is a financial executive with experience in investor relations, working with analysts, creditors and financial institutions, planning and analysis, capital allocation, SEC communications and reporting, accounting, acquisitions and turnarounds. He is experienced in effectively managing complex projects, building professional relations and developing staff. Mr. McGroarty was previously employed as CFO of Safeguard Scientifics, Interim Controller at Cephalon, Inc., Vice President-Financial Planning and Analysis of Exide Technologies, Inc., and Senior Manager at PWC. Jeff's MBA is from the Wharton School of Business.



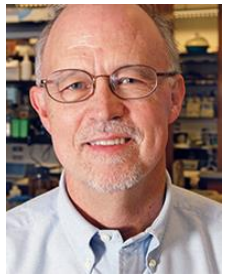
Jeffrey Cummings, MD, Chief Medical Advisor

Dr. Cummings completed Neurology residency and a Fellowship in Behavioral Neurology at Boston University, Boston, Massachusetts. US training was followed by a Research Fellowship in Neuropathology and Neuropsychiatry at the National Hospital for Nervous Diseases, Queen Square, London, England. Dr. Cummings was formerly Professor of Neurology and Psychiatry at UCLA, director of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA, director of the Deane F. Johnson Center for Neurotherapeutics at UCLA and director of the Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland and Florida. He is past president of the Behavioral Neurology Society and of the American Neuropsychiatric Association. Dr. Cummings has authored or edited 30 books and published nearly 600 peer-reviewed papers.

William Mobley, MD, PhD Chief Scientific Advisor

Distinguished Professor, Department of Neurosciences Florence Riford Chair for Alzheimer Research and Associate Dean for Neurosciences Initiatives. He is a member of the National Academy of Medicine. His research focuses on the neurobiology of neurotrophic factor actions/signaling and on the hypothesis that malfunction of these mechanisms contribute to neuronal dysfunction in developmental and age-related disorders of the neurosystem.

SCIENTIFIC ADVISORY BOARD



Sidney Strickland, PhD, Chairman

Vice President and Dean for Educational Affairs and Research Professor, Patricia and John Rosenwald Laboratory of Neurobiology and Genetics at Rockefeller University. Dr. Strickland's laboratory investigates how dysfunction of the circulatory system contributes to Alzheimer's and other neurodegenerative disorders. He will serve as the Chairman of Annovis Bio's SAB.

Peter Davies, PhD

Peter Davies received his B.Sc. and Ph.D. both in Biochemistry from the University of Leeds. He was a post-doctoral fellow at the University of Edinburgh, Scotland before joining the staff of the Medical Research Council Brain Metabolism Unit in Edinburgh in 1974, where he began his research on Alzheimer's disease. He is presently the Director of the Litwin-Zucker Research Center.

William Mobley, MD, PhD

Dr. Mobley is Distinguished Professor, Department of Neurosciences Florence Riford Chair for Alzheimer Research and Associate Dean for Neurosciences Initiatives. He is a member of the National Academy of Medicine. His research focuses on the neurobiology of neurotrophic factor actions/signaling and on the hypothesis that malfunction of these mechanisms contribute to neuronal dysfunction in developmental and age-related disorders of the neurosystem.

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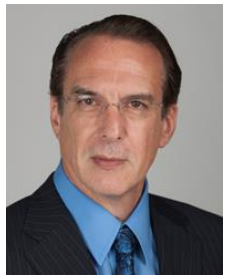
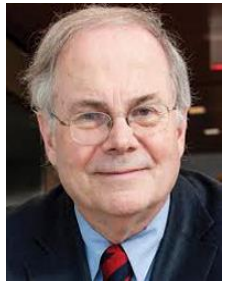


Gregory Petsko, PhD

He is a member of the National Academy of Sciences, the National Academy of Medicine, the American Academy of Arts and Sciences and the American Philosophical Society. His research interests are directed towards understanding the biochemical bases of neurological diseases like Alzheimer's, Parkinson's, and ALS discovering treatments (especially by using structure-based drug design), that could therapeutically affect those biochemical targets, and seeing any resulting drug candidates tested in humans. He has also made key contributions to the field of protein crystallography.



Rudolph E. Tanzi, PhD

Dr. Tanzi has published over 500 research papers and has received the highest awards in his field, including the Metropolitan Life Foundation Award, Potamkin Prize, Ronald Reagan Award, Silver Innovator Award, and many others. He was named to TIME magazine's list of TIME100 Most Influential People in the World (2015), and received the Smithsonian American Ingenuity Award, the top national award for invention and innovation. He co-authored the popular trade books "Decoding Darkness", New York Times bestseller, "Super Brain", and international bestseller "Super Genes".

BOARD OF DIRECTORS

Michael B. Hoffman
Chairman

Mr. Hoffman is the Founder and Managing Partner of Stone Capital Partners, a private equity firm focused on power and renewable energy. He was Partner of Riverstone, senior managing director at the Blackstone Group and managing director at Smith Barney, Harris Upham & Co. He serves as Chairman of Onconova, Annovis Bio, Curative and is on the Board of Rockefeller University.

Claudine E. Bruck, PhD

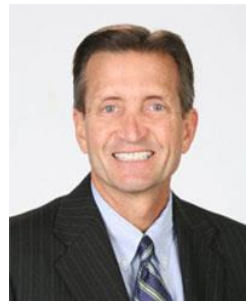
Pharmaceutical executive and scientist with strong entrepreneurial drive. Exhibited successes in building a therapeutic research unit de novo and leading discovery and clinical development of biological (vaccines, biopharmaceuticals) and small molecule medicines as well as an ophthalmic drug portfolio. With creativity and a strong results-focus, she is energized to challenge and lead teams. Extensive Pharmaceutical industry experience spans drug discovery and development across several therapeutic.

Maria L. Maccecchini, PhD
Executive Board Member

Founded Annovis in May 2008 to develop better therapeutics for Alzheimer's, Parkinson's and other neurodegenerative diseases. Founder and CEO of Symphony Pharmaceuticals/Annovis focused on protecting brain cells after stroke. It sold in 2001 to Transgenomic.

Mark White

Mark is a biopharmaceutical executive with global marketing, business development and sales experience. Currently, Mark is an independent consultant and a member of Robin Hood Ventures, a Philadelphia based angel investor group. Previously, Mark held senior level roles at Pfizer in marketing and commercial development, where he led the successful global launches of Inspira, Revatio, Lyrica and Xeljanz. In his last position, he was Vice President Worldwide Marketing, with global responsibility for new product development and in-line marketing for Pfizer's Inflammation Therapeutic Area.



Robert M. Whelan, Jr.

Mr. Whelan brings over 35 years of corporate finance and investment banking experience to Annovis' Board of Directors. Since 2001, Mr. Whelan has been President of Whelan & Company, LLC, providing financial consulting, valuation and strategic services to public and private companies in the technology, healthcare and alternative energy industries. From 1999 to 2001, Mr. Whelan served as Vice Chairman, Prudential Volpe Technology Group. Prior to then, Mr. Whelan was a senior executive with Volpe Brown Whelan, a private technology and healthcare investment banking, brokerage and asset management firm.

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INVESTMENT SUMMARY

A novel approach to treat neurodegeneration is desperately needed

- The markets for AD and PD drugs are in the multibillions of dollars and growing
- Annovis has a novel solution to stop the course of AD and PD
- ANVS401 improves axonal transport and homeostasis in the brain and recovers the affected function
- The successful completion of our two Phase 2a studies will provide optimal information on target and pathway engagement in AD and PD and allows us to move to two Phase 3 studies

ANNOVIS

Improves **THE FLOW** of Axonal Transport in Alzheimer's Disease and Neurodegeneration

ANVS401 ANVS405 ANVS301

Symbol: **ANVS** (NYSE American)

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