



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

Axonal Transport

Symbol: **ANVS** (NYSE American)

July 2021



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 projected timelines of clinical trials, and expectations regarding current or future clinical trials. 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, including that clinical trials may be delayed; that the data reported herein is interim data, conclusions as to which may be superseded by subsequent data we expect to receive in connection with Phase 2a trials and/or subsequent clinical trials; and that any anticipated meeting with or presentation to the FDA may be delayed. 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, 2020 and other reports 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

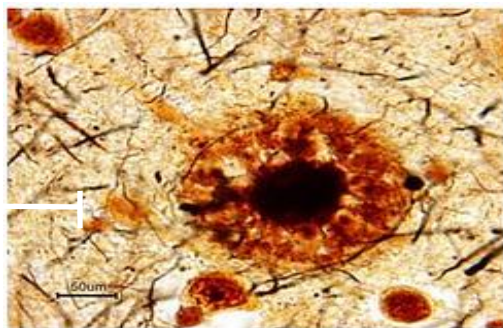
- **Annovis is developing drugs** for Alzheimer's (AD) and Parkinson's disease (PD), including the orphan indication Alzheimer's in Down Syndrome (AD-DS)
- **Lead compound - ANVS401 - in Phase 2a clinical trial**, is the only drug to improve cognition in AD and motor function in PD patients, as recently announced
- **ANVS401 reduced inflammation**, in PD patients as recently announced. Additional biomarker data to come.
- **Successful completion of phase 2a clinical trials** will validate our approach and allow start of two phase 3 studies

ANNOVIS' NEW APPROACH TO ATTACK AD AND PD

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

Amyloid β

Alzheimer's - Parkinson's
 $A\beta$ Targeting Compounds



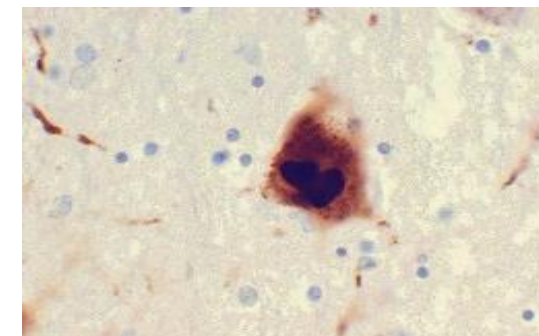
Tau

Tauopathies - Alzheimer's
Tau Targeting Compounds



α Synuclein

Parkinson's - Alzheimer's
 α SYN Targeting Compounds



Attacking one neurotoxic protein results in minimal effect

ANVS401 is the only drug to attack multiple neurotoxic proteins simultaneously



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

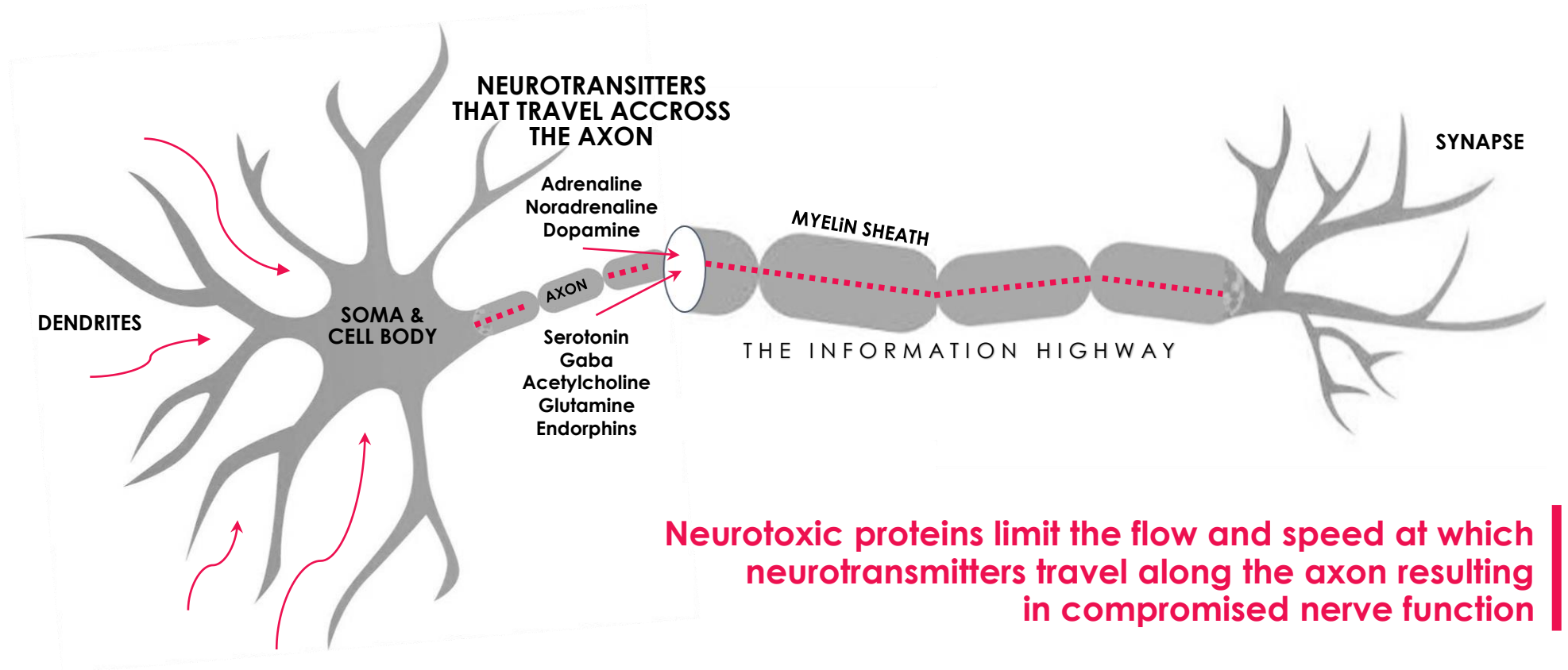
IMPROVED COGNITIVE AND
MOTOR FUNCTION

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



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

NEURODEGENERATION IS AN AXONAL TRANSPORT DISEASE

“Axonal transport disruption is linked to human neurological conditions.” - Nature Review, September 2019

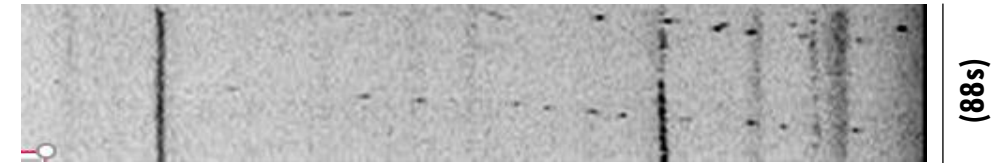
Axonal transport is responsible for:

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

← Retrograde (0.5 frame/sec) →

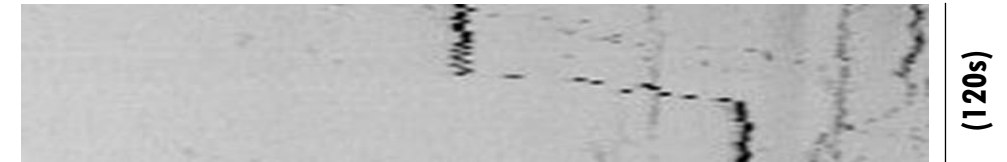
Normal Transport

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

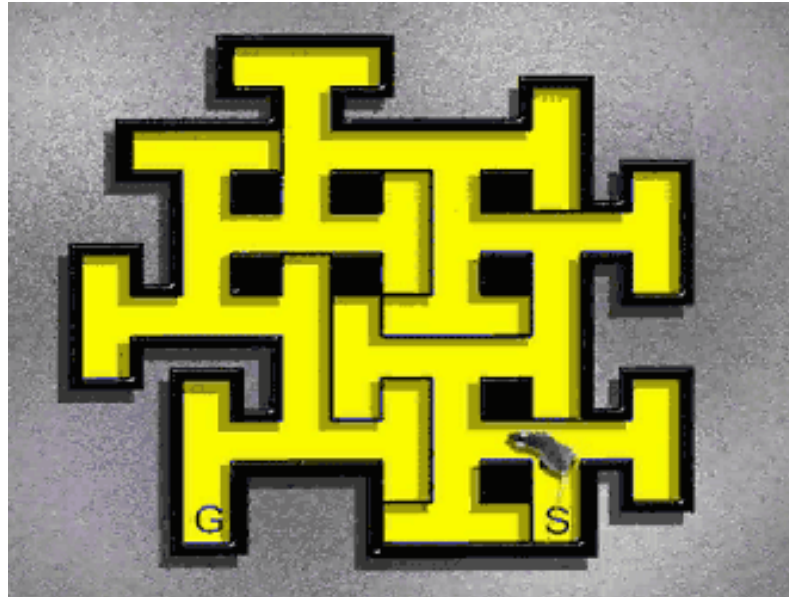
The **Flow and Speed** of axonal transport is improved.



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

RESULTS IN ANIMALS

Multiple animal studies showed that ANVS401 improved the affected function



Function

Memory and learning (4)

Movement (2)

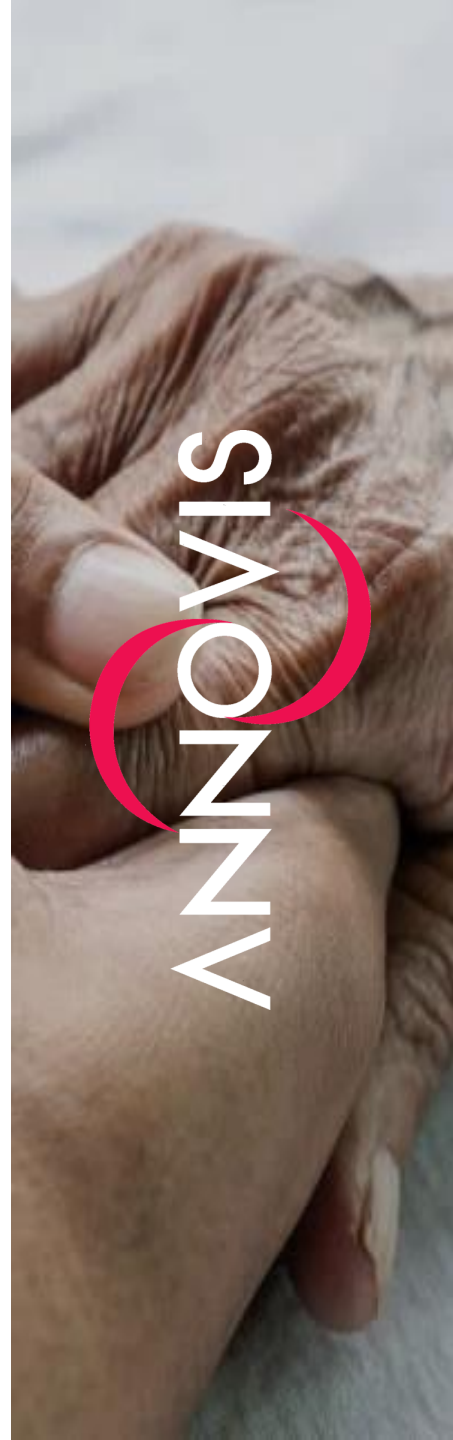
Eyesight (1)

Animal Model

AD mice, DS mice, stroke mice, TBI rats

PD mice, FTD mice

Acute glaucoma rats



TWO PHASE 2 CLINICAL TRIALS

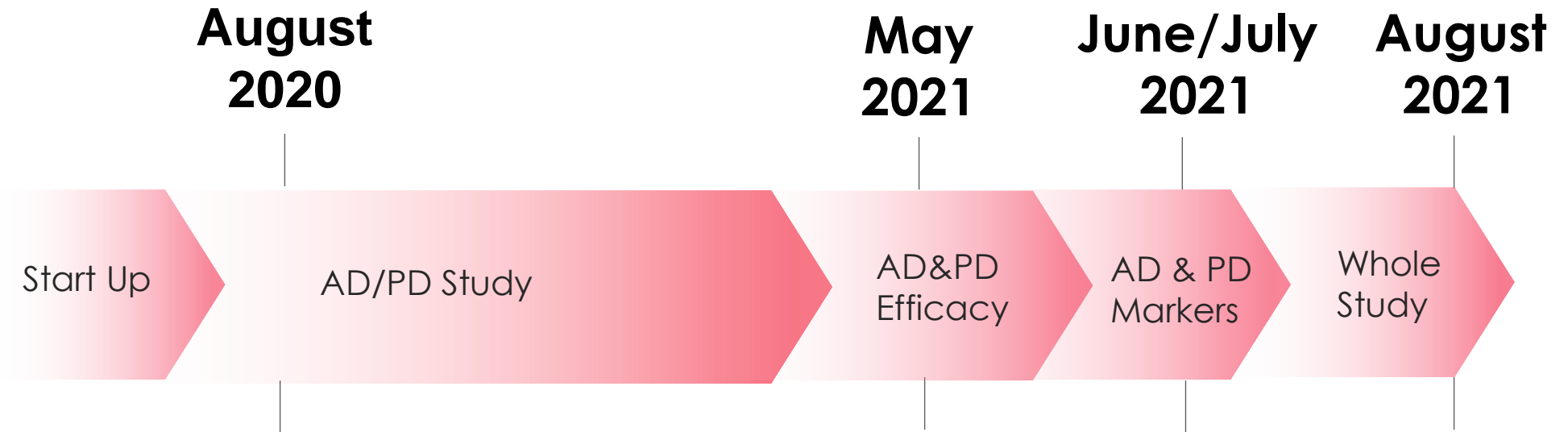
AD Trial

PD Trial

CRO	Parexel	
Therapeutic Area	Early to Moderate AD	Early to Moderate PD
Phase	2	2
Patients	14	14 + 40
Sites	12	12
Country	United States	
Design	Double-Blind, Placebo-Controlled, Biomarker Study	
Endpoints	Reversal of Toxic Cascade	

TIMELINE OF PHASE 2 CLINICAL TRIAL IN AD and PD

Preliminary data commenced in 1Q2021



A meeting with the FDA to discuss the data from the AD and the PD study as well as from the chronic toxicology in rats and dogs is projected for Fall of 2021



REVERSAL OF TOXIC CASCADE

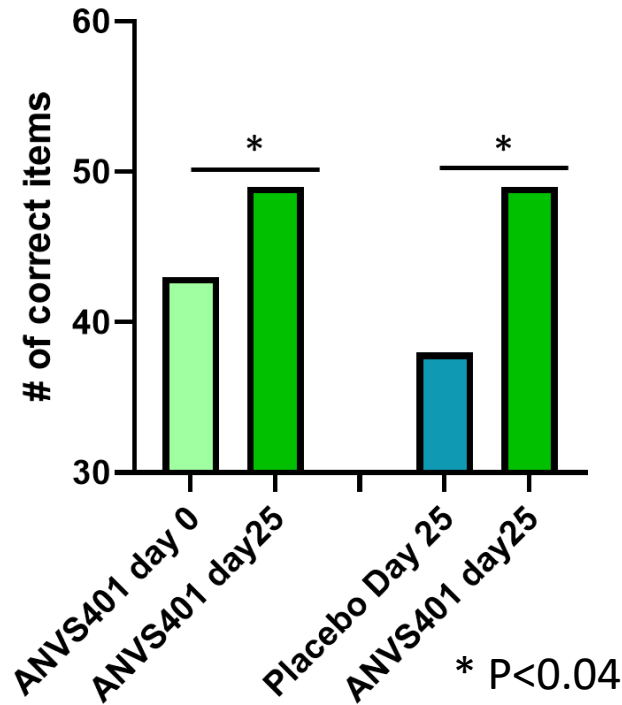
Data from first 14 AD and 14 PD patients

REVERSAL OF TOXIC CASCADE	EXPECTED OUTCOME	ACTUAL OUTCOME	
		AD	PD
Level of neurotoxic proteins	↓		
Axonal transport	↑		
Inflammation	↓		+++
Dead nerve cells	↓		
Control proteins	0		
Efficacy: WAIS coding	↑	+	+
Efficacy: Motor function	↑		+
Efficacy: Cognition	↑	+	

+++ $p \leq 0.001$
++ $p \leq 0.01$
+ $p \leq 0.05$
+/- trend
0 no change
- opposite result from expected

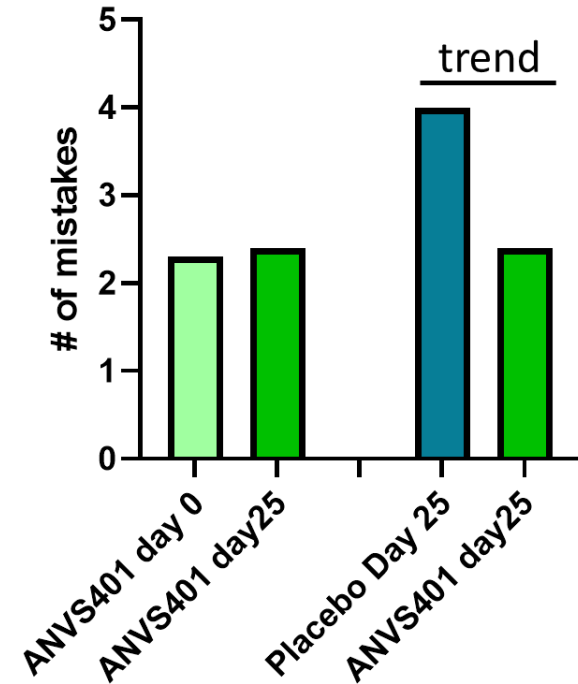
EFFICACY IN PD PATIENTS – SPEED & COORDINATION

Data from first 14 PD patients



Speed: Left - the comparison between the treated group with 80 mg/day of ANVS401 at baseline before treatment and after 25 days on treatment in the rapid coding test. At 25 days the speed is faster than at baseline and they make fewer mistakes ($p<0.04$).

Right - the comparison between the placebo group and the treated group at 25 days. This graph shows that while the placebo group gets slower, the treated group gets faster ($p<0.04$). The lower number shows worse performance.



Coordination: Left - Comparison between treated at baseline and at 25 days. The two scores are identical – patients remain stable

Right - the comparison is made between the placebo group and the treated group both at 25 days. The placebo treated group shows a marked deterioration in their motor complications compared to the ANVS401 treated group that was stable ($p<0.07$). The lower number shows better performance.

LOWERING OF INFLAMMATION IN PD PATIENTS

Data from first 14 PD patients

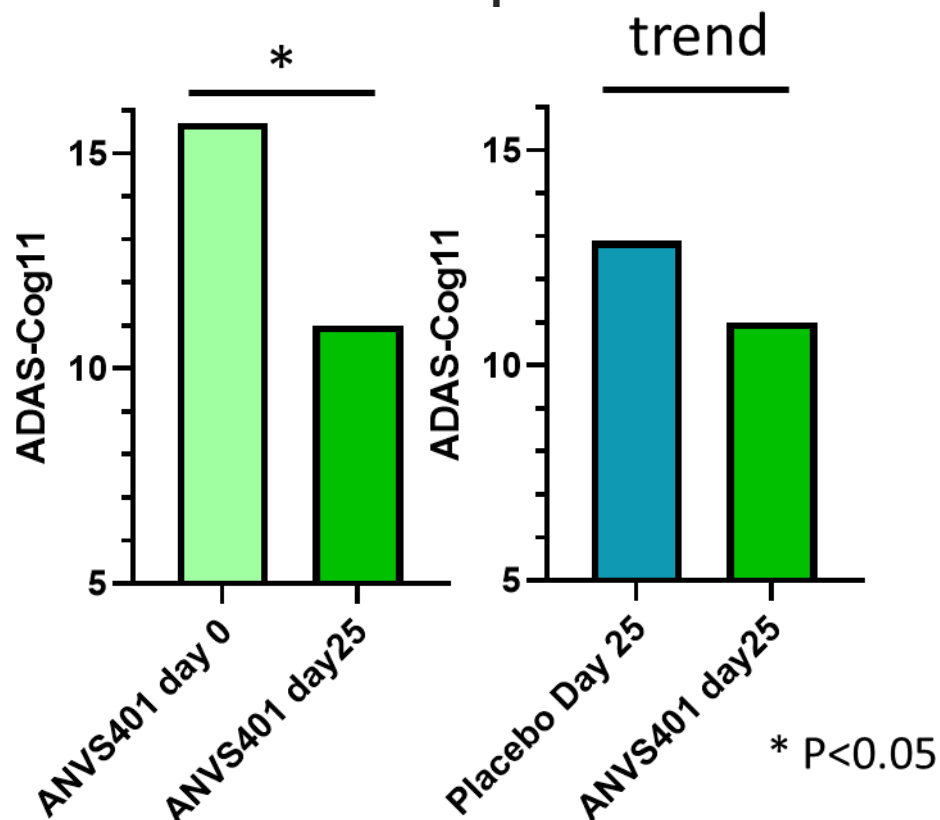
Inflammatory Marker	% Change from Baseline	p-Value
Complement C3	-24.9	0.0072
YKL40	-22.9	0.0213
sTREM2	-28.2	0.0108
GFAp	-34.6	0.000001

The trial measured four inflammatory markers that are prevalent in the brains of AD and of PD patients.

Each of the inflammatory markers showed statistically significant reduction after 25 days of treatment with ANVS401 compared to baseline.

EFFICACY IN AD PATIENTS – ADAS-Cog11

Data from 14 AD patients



Within Data:

From baseline to 25 days in the ANVS401-treated group, ADAS-Cog11 improved by 4.4 points, a statistically significant improvement of 30% ($p<0.05$).

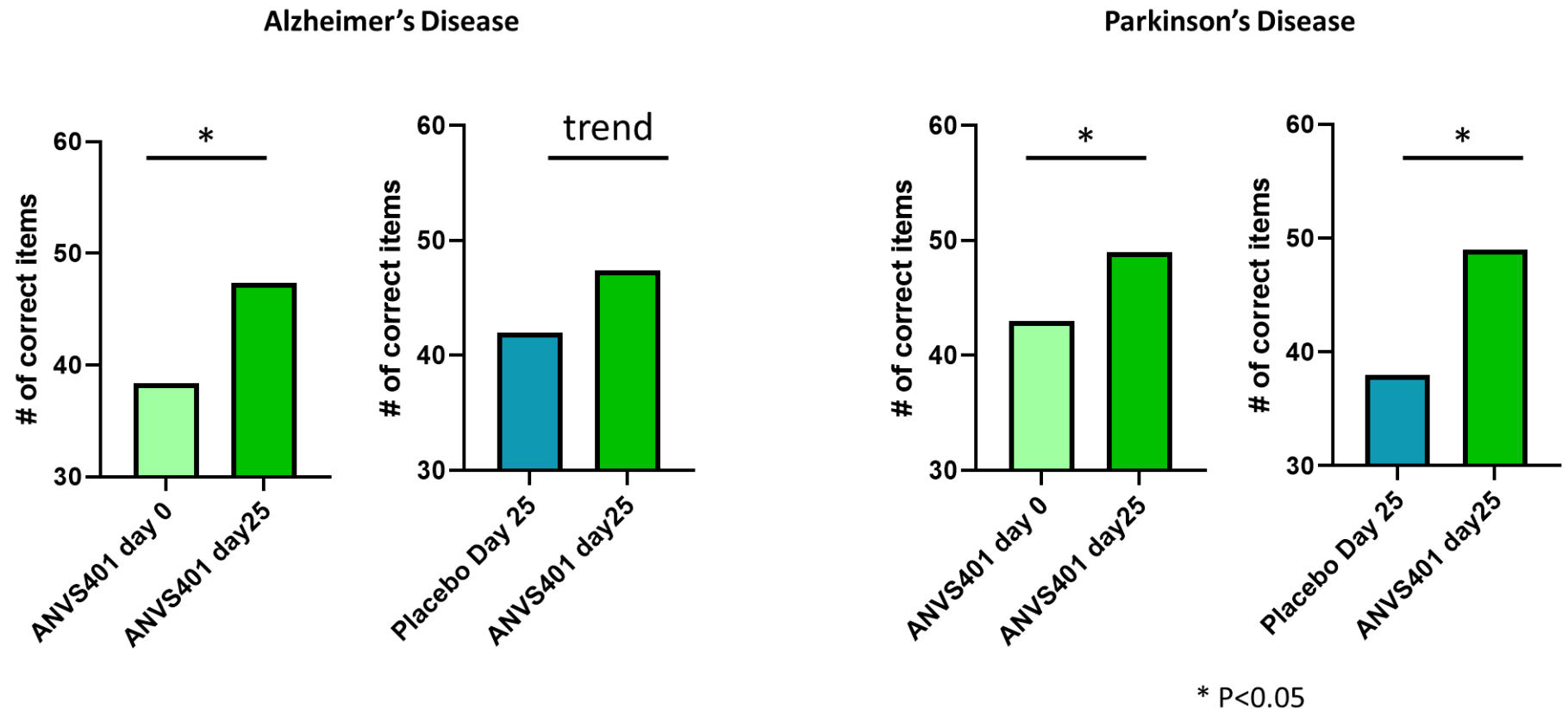
Between Data:

ANVS401-treated group compared to placebo group at 25 days showed an improvement of 3.3 points, or 22% ($p=0.13$).

This is the first double-blind, placebo-controlled study that shows cognitive improvements in AD patients as measured by ADAS-Cog and functional improvements in PD patients as measured by the Unified Parkinson's Disease Rating Scale (UPDRS).

CODING TEST SHOWS SIMILAR IMPROVEMENT IN AD AND PD PATIENTS

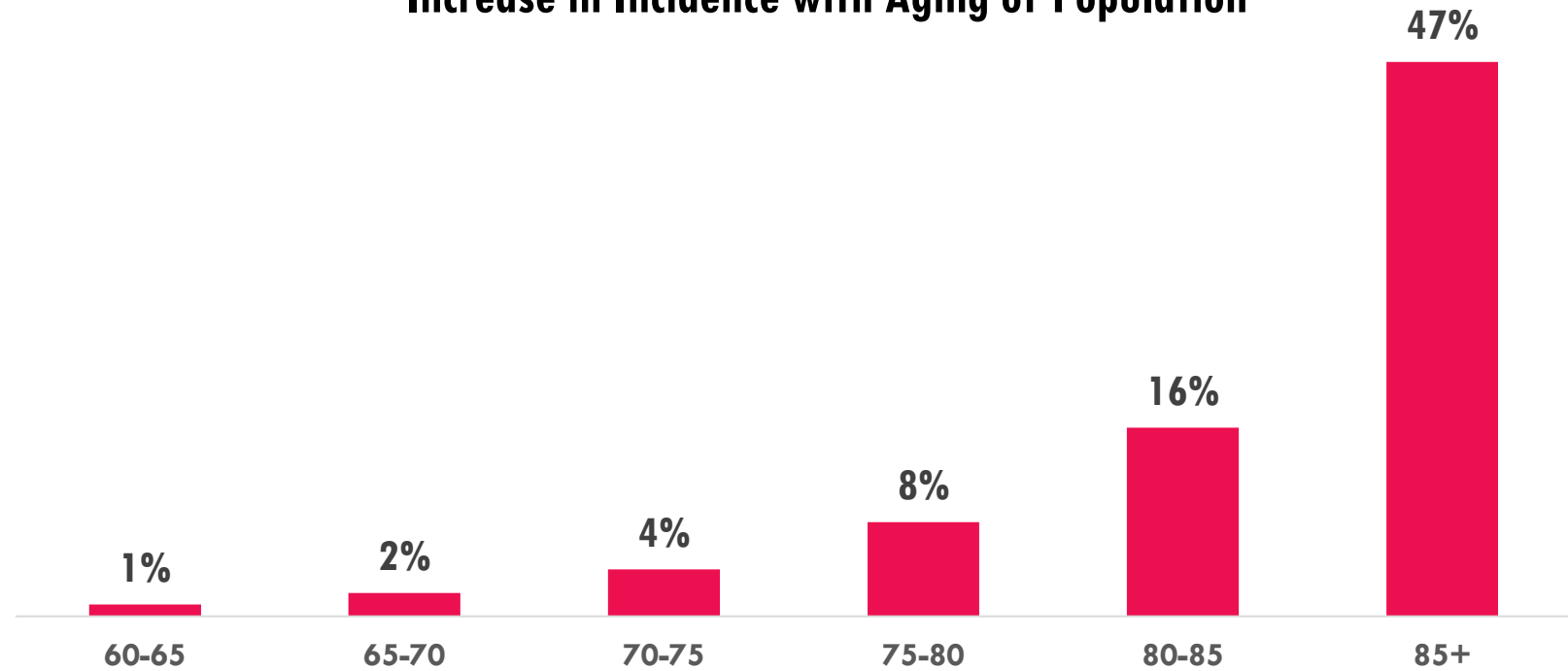
WAIS Results



The WAIS coding test measures speed in movement and thinking. Treated AD patients show a 6.6 point and PD patients a 6.1-point improvement in coding after ANVS401 treatment.

MARKET PROJECTIONS

Increase in Incidence with Aging of Population



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

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

The left side of the slide features a vertical image of several test tubes in a rack, with a pair of blue gloves holding one. The Annovis logo, consisting of the word 'ANNOVIS' in white capital letters with a red swoosh, is overlaid on the image.

FINANCIAL HIGHLIGHTS

- IPO in January 2020
- Completed \$50M equity raise in May 2021
- Fully funded through anticipated Phase 3 trial / two years
- NIH grants funding ADCS Phase 2a trial in AD and chronic toxicology study
- ~38% insider ownership
- Analyst coverage from ThinkEquity and Maxim Group

KEY DATA

Ticker	NYSEAmerican: ANVS
Recent Price	\$85.58
52-Week Range	\$3.84 - \$100.97
Market Cap	\$692M
Shares Outstanding	8.1M
Float	5.6M
Cash	\$49M
LT Debt	\$0.0M

Share price, market cap, cash & debt as of June 30, 2021

MANAGEMENT AND ADVISORY TEAM



Maria L. Maccocchi, PhD, Founder, President & CEO

Dr. Maccocchi 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. Maccocchi 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

Mr. McGroarty 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. His MBA is from the Wharton School of Business.



Cheng Fang, PhD, VP of Research

Dr. Fang is an experienced neuroscientist with more than a decade of experience in neurodegenerative diseases, with broad scientific knowledge and hands-on experience. Prior to joining Annovis, she was a scientific solution consultant with Clarivate Analytics where she worked on cutting-edge scientific projects with top-50 pharma clients. Previously, Dr. Fang was business development manager for Coriell Institute for Medical Research and an assistant professor at Boston University, where she designed and supervised projects focused on prion diseases and AD as a research team leader.



William Mobley, MD, PhD, Chief Scientific Advisor

Distinguished Professor, Department of Neurosciences Florence Riford Chair for Alzheimer Research and Associate Dean for Neurosciences Initiatives at UC San Diego. 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.

Gregory Petsko, PhD



Dr. Petsko 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.

Jeffrey Cummings, MD



Dr. Cummings completed Neurology residency and a Fellowship in Behavioral Neurology at Boston University, Massachusetts. US training was followed by a Research Fellowship in Neuropathology and Neuropsychiatry at the National Hospital for Nervous Diseases, London, England. Dr. Cummings was formerly Professor of Neurology and Psychiatry, Director of Alzheimer's Disease Research and Director of the Center for Neurotherapeutics at UCLA. He was Director of the Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland and Florida.

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.



Maria L. Maccocchi, PhD
Executive Board Member

Dr. Maccocchi founded Annovis in May 2008 to develop better therapeutics for Alzheimer's, Parkinson's and other neurodegenerative diseases. She was the Founder and CEO of Symphony Pharmaceuticals/Annovis, a company focused on protecting brain cells after stroke which was sold in 2001 to Transgenomic.



Reid S. McCarthy

Mr. McCarthy is experienced in corporate financial management, operations and new venture development. He was CFO of Topaz Pharmaceuticals, Inc. until its sale in 2011 to Sanofi Pasteur. He also served as CFO of JJ Haines & Company, Inc. and provided consulting CFO services to several life sciences companies. He has been a founding executive of several venture capital-backed companies which were successfully sold.

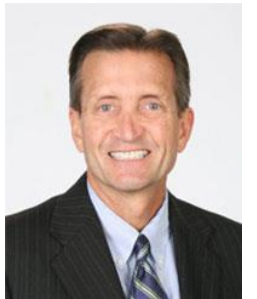
Claudine E. Bruck, PhD

Dr. Bruck is a 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 areas.



Mark White

Mr. White is a biopharmaceutical executive with global marketing, business development and sales experience. Currently, he is an independent consultant and a member of Robin Hood Ventures, a Philadelphia based angel investor group. Previously, Mr. White 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.





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 approach to stop AD and PD
- ANVS401 shows statistically significant improvements in Phase 2a clinical trials:
 - Cognition in AD patients
 - Motor function in PD patients
 - WAIS coding in AD and PD patients
 - Inflammation in PD patients
- The successful completion of our Phase 2 clinical trials is providing validation of our approach in two diseases and allow us to move to Phase 3 trials in both diseases

CHANGE IN CAUSES OF DEATH FROM 2000 TO 2018

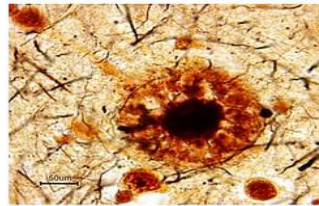
- Breast Cancer - 13%
- Colon Cancer - 21%
- Heart Disease - 21%
- Stroke - 24%
- HIV - 67%
- Parkinson's + 84%
- Alzheimer's + 112%

ANNOVIS' DRUG ATTACKS MULTIPLE NEUROTOXIC PROTEINS

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

Amyloid β

AD / PD - A β Targeting Compounds



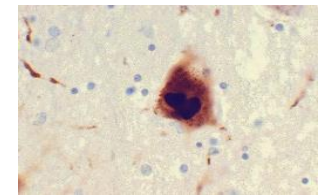
Tau

Tauopathies - AD - Tau Targeting Compounds

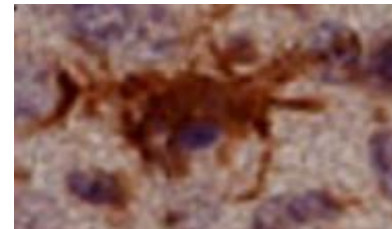


α Synuclein

PD / AD - α SYN Targeting Compounds



Activated Microglia = High Inflammation



Attacking one neurotoxic protein results in minimal effect

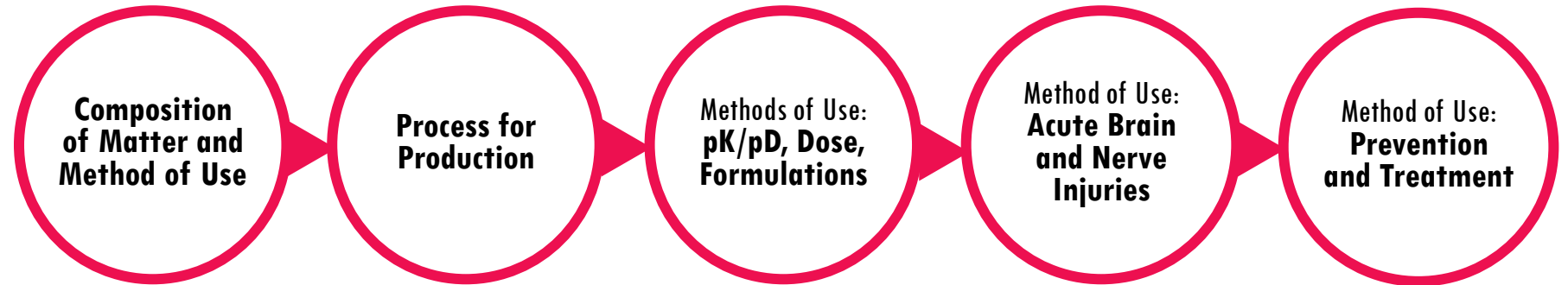
ANVS401 is the only drug to attack multiple neurotoxic proteins simultaneously

PIPELINE

Therapy	Diseases/Conditions	PRE-CLINICAL	IND	PHASE I	PHASE II	PHASE III
<div>ANVS401</div> <div>Oral drug for chronic indications</div>	AD					
	PD					
	AD-DS					
	FTD					
	CTE					
<div>ANVS405</div> <div>Injectable drug for acute traumatic events</div>	TBI					
	Stroke					
<div>ANVS301</div> <div>Oral drug for advanced AD and dementia</div>	Advanced AD					

CORPORATE PATENT ESTATE

Multi-layer strategy



Patent/Application	Subject Matter	Status	Expiry
Provisional	ANVS401 to treat viral and bacterial infections of the brain, including Covid19	Pending	2042
PCT	ANVS401 and 405 – Mechanism of Action for prevention and treatment of diseases	Pending	2038
PCT	ANVS405 - Acute brain and nerve injuries	Granted – Europe and Japan	2036
PCT	ANVS401 - pK/pD, low doses, formulations Neurodegenerative Diseases	Granted – US and Europe	2031
In-licensed patents	Composition of matter, manufacturing, method for treating AD and DS	Granted	2022-25



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

ANVS401 **ANVS**405 **ANVS**301

Symbol: **ANVS** (NYSE American)

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