

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549**

FORM 8-K

**CURRENT REPORT
Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934**

Date of report (Date of earliest event reported): March 23, 2021

ANNOVIS BIO, INC.

(Exact Name of Registrant as Specified in Charter)

**Delaware
(State or Other Jurisdiction
of Incorporation)**

**001-39202
(Commission
File Number)**

**26-2540421
(I.R.S. Employer
Identification No.)**

**1055 Westlakes Drive, Suite 300
Berwyn, PA 19312
(Address of Principal Executive Offices, and Zip Code)**

**(610) 727-3913
Registrant's Telephone Number, Including Area Code**

Not Applicable

(Former Name or Former Address, if Changed Since Last Report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	ANVS	NYSE American

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

- Written communication pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communication pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communication pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

On March 24, 2021, as part of the Q1 Investor Summit, Chief Executive Officer Maria Maccicchini, Ph.D., and Chief Financial Officer Jeff McGroarty, MBA, CPA, will give a presentation via webcast at 11:30 a.m. Eastern Time, followed by a live Q&A session. A copy of the written presentation materials is attached as Exhibit 99.1 to this Current Report on Form 8-K. A copy of the presentation is also available on the Company's website at www.annovisbio.com under "Investors & Media." Investors can register for and access the live webcast at: https://zoom.us/webinar/register/WN_LKCiDrrKROa4nLfrPKSiAA

The information in this Item 7.01, including the attached exhibit, is furnished solely pursuant to Item 7.01 of Form 8-K. Consequently, such information is not deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liabilities of that section. Further, the information in this Item 7.01, including the exhibit, shall not be deemed to be incorporated by reference into the filings of the registrant under the Securities Act of 1933.

Cautionary Statement Regarding Forward-Looking Information

This current report on Form 8-K contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than those of historical fact in this presentation and accompanying oral commentary are forward-looking statements. Forward-looking statements may be identified by terminology such as "believe," "anticipate," "plan," "may," "intend," "will," "should," "expect," "estimate," "potential" and "continue" and similar expressions, including the negative of these words, but not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements regarding the Company's expectations regarding projected timelines of clinical trials, and expectations regarding current or future clinical trials. Forward-looking statements are based on the Company'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 the timing of clinical trials. 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 filed with the Securities and Exchange Commission ("SEC") and elsewhere in our filings and reports with the SEC. These risks, uncertainties and other factors may cause our actual results to differ materially and adversely from what is contained in (or may be implied from) any forward-looking statements. Forward-looking statements speak as of the date they are made, and the Company undertakes no obligation to update them except as may be required under applicable law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Presentation dated March 2021 (furnished herewith)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ANNOVIS BIO, INC.

Date: March 23, 2021

By: /s/ Jeffrey McGroarty

Name: Jeffrey McGroarty

Title: Chief Financial Officer

The logo for ANNOVIS features the word "ANNOVIS" in a white, sans-serif font. A red, stylized circular graphic element, resembling a partial ring or a path, is positioned behind the letters "NNO", partially overlapping them.

ANNOVIS

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

Axonal Transport

Symbol: **ANVS** (NYSE American)

March 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 the timing of clinical trials. 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 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 clinical trials:**
 - AD trial run by Alzheimer's Disease Cooperative Study (ADCS)
 - AD and PD trial
- **Successful completion of phase 2a clinical trials** will validate our approach and allow start of two phase 3 studies



THE STATE OF NEURODEGENERATIVE DISEASES

- 5.8 million people in the US and 44 million people worldwide are estimated to suffer from AD
- PD affects an estimated one million people in the U.S. and as many as 10 million globally
- Total costs of care for people with Alzheimer's and other dementias could top \$1.1 trillion in 2050
- From 1998 to 2018 there were over 500 failed attempts at developing Alzheimer's drugs, primarily focused on amyloid plaque
- The sector needs to rethink dementia, develop new approaches and create new drugs

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%

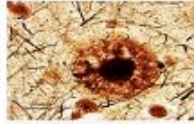


ANNOVIS' DRUG ATTACKS MULTIPLE NEUROTOXIC PROTEINS

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

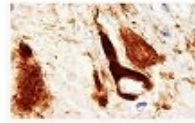
Amyloid β

AD/ PD-A β Targeting Compounds



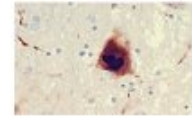
Tau

Tauopathies-AD-Tau Targeting Compounds

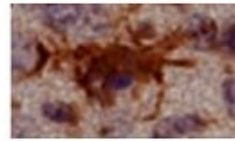


α Synuclein

PD/ AD- α SN 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
ANVS401 Oral drug for dementias	AD	[Progress bar]				
	PD	[Progress bar]				
	AD-DS	[Progress bar]				
	FTD	[Progress bar]				
	CTE	[Progress bar]				
ANVS405 Injectable drug for acute traumatic events	TBI	[Progress bar]				
	Stroke	[Progress bar]				
ANVS301 Oral drug for advanced AD/dementia	Advanced AD	[Progress bar]				



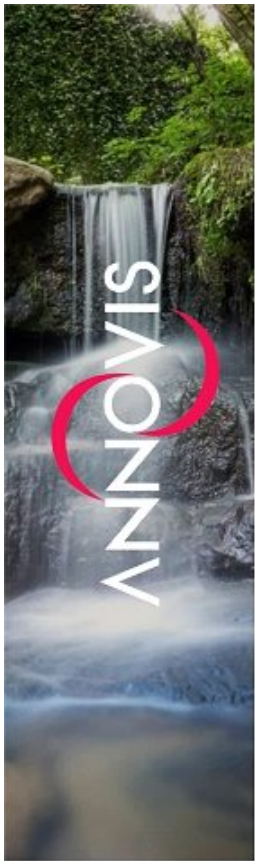
CORPORATE PATENT ESTATE

Multi-layer strategy



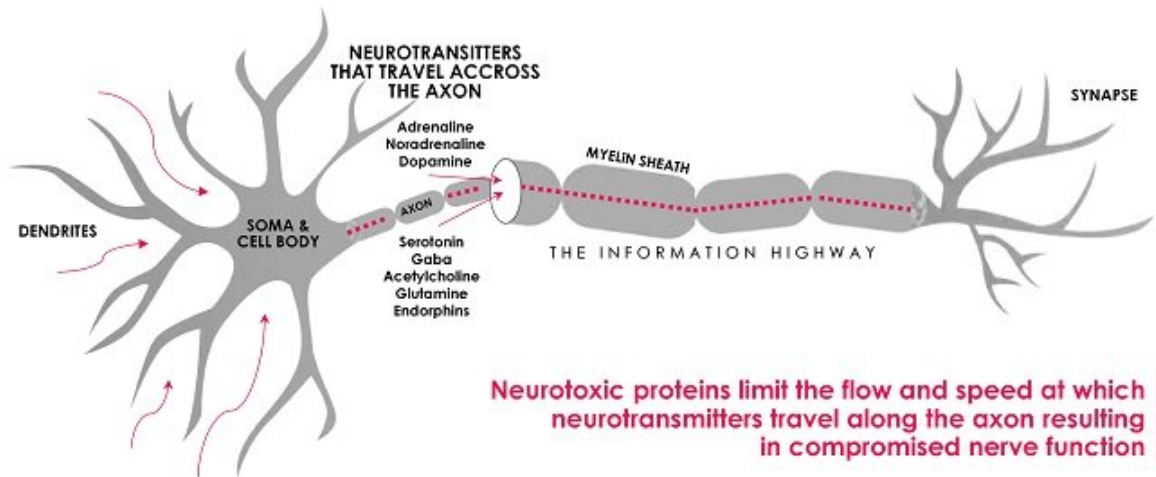
Patent/Application	Subject Matter	Status	Expiry
Provisional	ANVS401 to treat viral and bacterial infections of the brain, including Covid19	Pending	2041
PCT	ANVS401 and 405 – Mechanism of Action for prevention and treatment of diseases	Pending	2038
PCT	ANVS405 - Acute brain and nerve injuries	EP 3334425B1; 12-2020	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 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

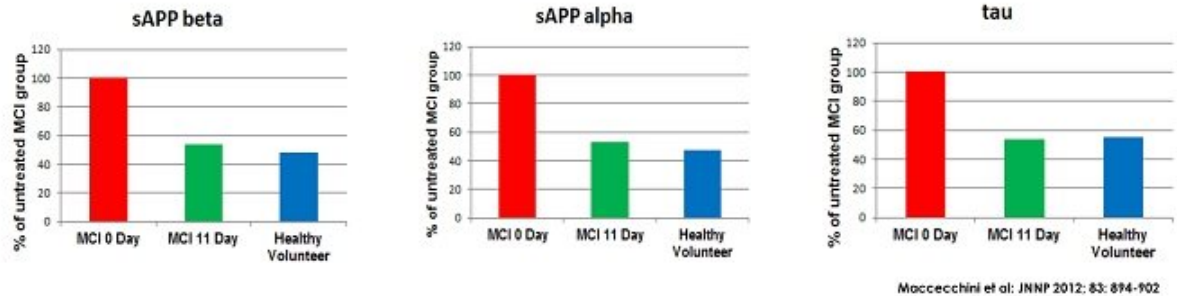
IMPROVED COGNITIVE AND
MOTOR FUNCTION

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



RESULTS IN HUMANS

ANVS401 Lowers Neurotoxic Proteins in Cerebrospinal Fluid (CSF) of Mild Cognitive Impaired (MCI) Patients



- In this proof-of-concept study, ANVS401 lowers the levels of APP/A β , tau/p-tau and α SYN 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 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 ANVS 401

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



APP, Aβ42, C9 – Mtbly; LCO, αSN – Issach, Harvard, Lee, URMt
Tβu – U.Manch & Zurich; Ht – Mtbly; LCO, ERG – Tyla, Northwestern



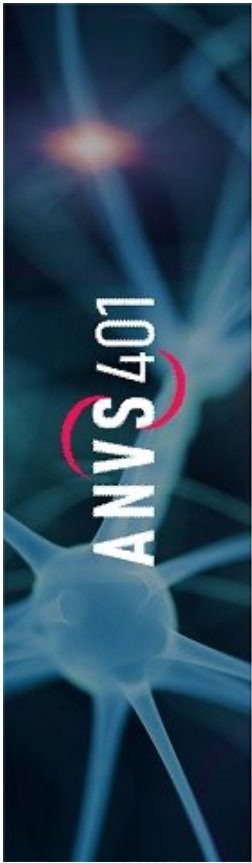
ANVS401 LOWERS INFLAMMATORY MARKERS

**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

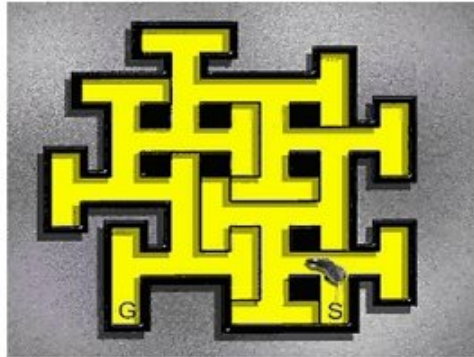
* Ctrlrd Factor

Macedini et al. JNP2012;83:894-902



RESULTS IN ANIMALS

Multiple animal studies showed that ANVS401 improved the affected function



Function

Memory and learning

Movement

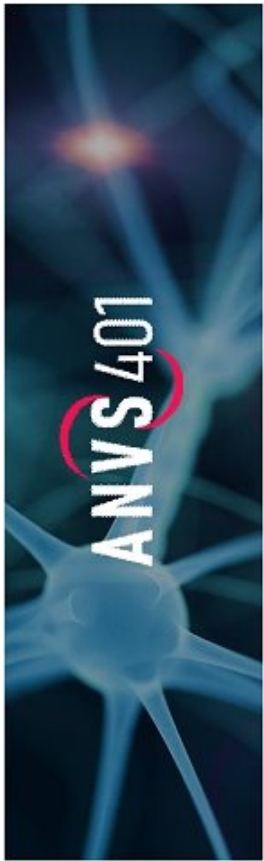
Eyesight

Animal Model

AD mice, DS mice, stroke mice, TBI rats

PD mice, FTD mice

Acute glaucoma rats





TWO PHASE 2 CLINICAL TRIALS

	AD Trial	AD / PD Trial
CRO	ADCS	Parexel
Therapeutic Area	Early AD	Early to Moderate AD and PD
Phase	2	2
Patients	24	28 + 40
Sites	6	12
Country	United States	
Design	Double-Blind, Placebo-Controlled, Biomarker Study	
Endpoints	Reversal of Toxic Cascade	



PHASE 2 CLINICAL TRIAL IN AD AND PD TO
MEASURE REVERSAL OF THE TOXIC CASCADE
AND IMPROVEMENT IN BRAIN FUNCTION

ENDPOINTS

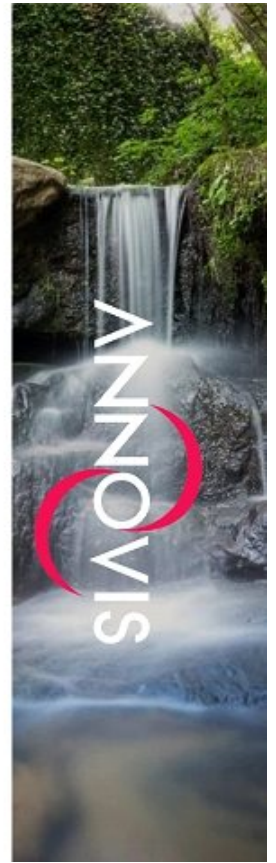
TARGET: DECREASE IN NEUROTOXIC PROTEINS

PATHWAY: INCREASE IN NEUROTRANSMITTERS

LOWERING OF INFLAMMATORY PROTEINS

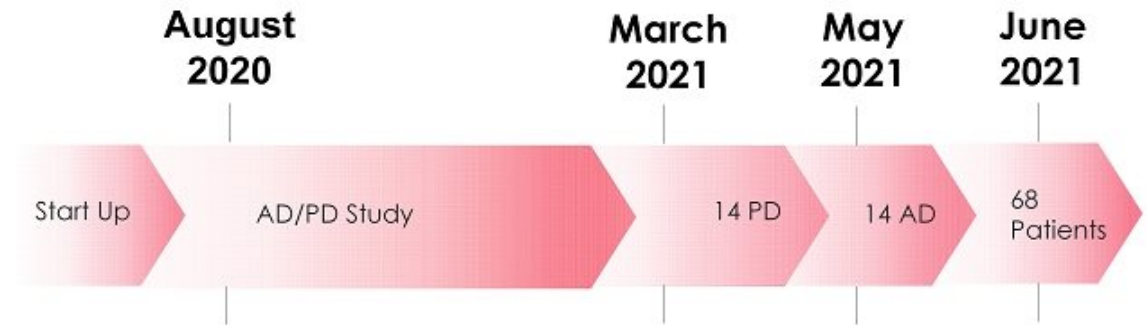
LOWERING OF NEURODEGENERATION
MARKERS

EFFICACY: COGNITION AND MOTOR FUNCTION



TIMELINE OF PHASE 2 CLINICAL TRIAL IN AD and PD

Preliminary data to be available beginning in 1Q2021

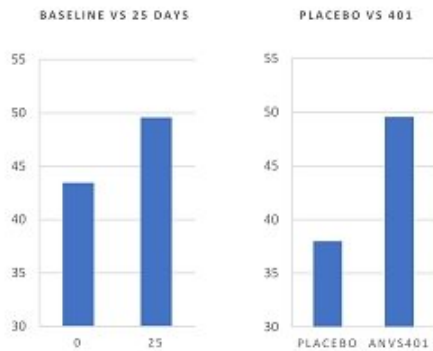


A meeting with the FDA to discuss the data from the AD and the PD study as well as from the chronic toxicology in rats and dogs is projected for Fall of 2021



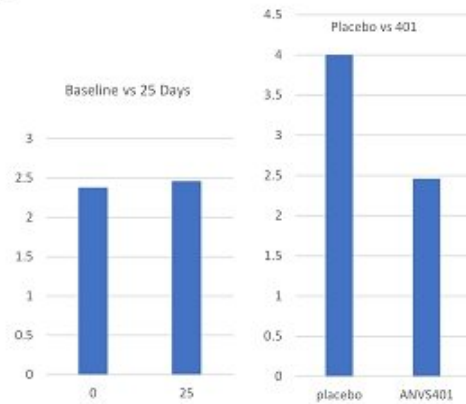
EFFICACY IN PD PATIENTS – SPEED & COORDINATION

Preliminary 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.



REVERSAL OF TOXIC CASCADE

Preliminary data from first 14 PD patients

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

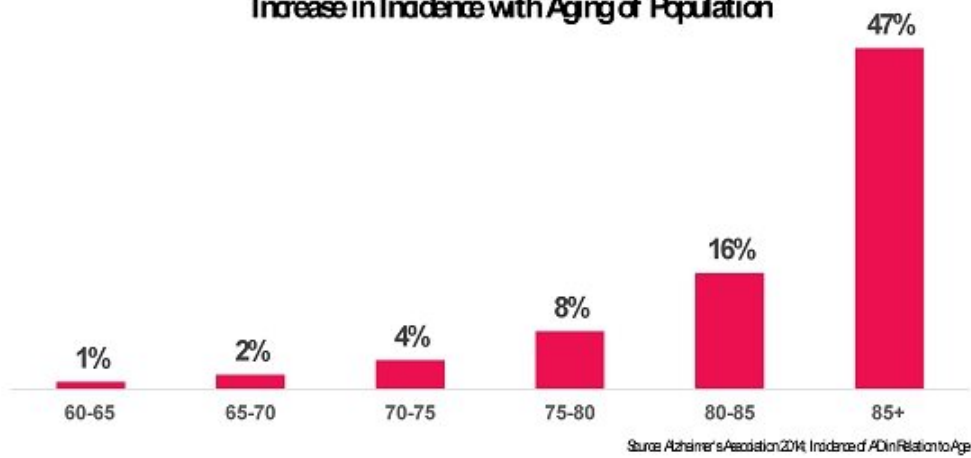
+++ $p \leq 0.001$
 ++ $p \leq 0.01$
 + $p \leq 0.05$
 +/- trend

0 no change
 - Opposite result from expected

All rows for Parkinson's disease will read out later and the same outcomes will also read out for Alzheimer's disease

MARKET PROJECTIONS

Increase in Incidence with Aging of Population



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



FINANCIAL HIGHLIGHTS

- Completed IPO in January 2020
- Cash balance provides runway to end of 2021
- NIH grants funding ADCS Phase 2a trial in AD and chronic toxicology study
- ~40% insider ownership
- Analyst coverage from ThinkEquity and Maxim Group

KEY DATA

Ticker	NYSEAmerican: ANVS
Recent Price	\$25.57
52-Week Range	\$2.42-\$35.00
Market Cap	\$176.6M
Shares Outstanding	6.9M
Float	4.4M
Cash (mrq)	\$8.8M
LT Debt (mrq)	\$0.0M

Share price and market cap as of February 26, 2021

CHIEF EXECUTIVES AND CHIEF ADVISORS



Maria L. Maccacchini, 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. Maccacchini 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 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.

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.

William Mobley, MD, PhD



Dr. Mobley is 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.

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 areas.

Maria L. Maccacchini, PhD
Executive Board Member

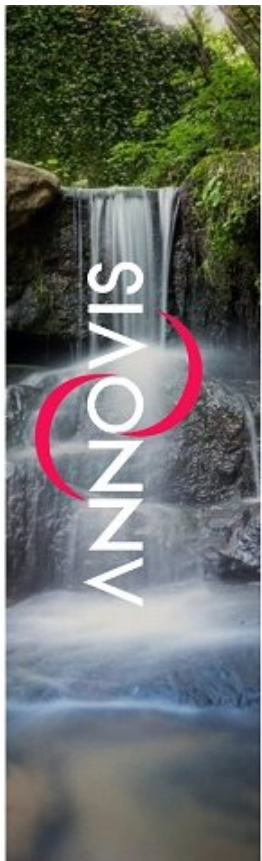
Founded Annovis in May 2008 to develop better therapeutics for Alzheimer's, Parkinson's and other neurodegenerative diseases. Founder and CEO of Symphony Pharmaceuticals/Annovis focused on protecting brain cells after stroke. It sold in 2001 to Transgenomic.



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.





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 approach to stop the course of AD and PD
- ANVS401 improves axonal transport and recovers the affected function
- The successful completion of our Phase 2 clinical trials will provide validation of our approach in two diseases and allow us to move to Phase 3 trials



ANNOVIS

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

ANVS401 **ANVS405** **ANVS301**

Symbol: **ANVS** (NYSE American)

CONTACT US

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