

**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): January 6, 2023

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	New York Stock Exchange

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 8.01 Other Events

On January 6, 2023, Annovis Bio, Inc. (the “Company”) posted a presentation to its website that may be used by the Company from time to time in meetings with investors, analysts, collaborators, vendors or other third parties. A copy of the presentation is attached as Exhibit 99.1 to this report and incorporated into this Item 8.01 by reference.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits.

The Company hereby files or furnishes, as applicable, the following exhibits:

Exhibit No.	Description
99.1	Presentation, dated January 6, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: January 6, 2023

By: /s/ Henry Hagopian, III
Name: Henry Hagopian, III
Title: Chief Financial Officer



- People Focused, Purpose Driven, Passion Powered -

Attacks Neurodegeneration, Alzheimer's and
Parkinson's Diseases by Improving the Information
Highway of the Nerve Cell

Symbol: **ANVS** (NYSE)

January 2023



FORWARD-LOOKING STATEMENTS

Forward Looking Statements and Other Important Cautions – This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements relate to all information other than historical matters, such as expectations or forecasts of future events. Forward-looking statements may be identified by the use of words such as “forecast,” “intend,” “seek,” “target,” “anticipate,” “believe,” “expect,” “estimate,” “plan,” “outlook,” and “project” and other similar expressions that predict or indicate future events or trends or that are not statements of historical matters. Forward-looking statements with respect to the operations, strategies, prospects and other aspects of the business of Annovis Bio are based on current expectations that are subject to known and unknown risks and uncertainties, which could cause actual results or outcomes to differ materially from expectations expressed or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: that clinical trials may be delayed; that the data reported herein is from a Phase 2a study and subsequent clinical trials are being conducted; and that any anticipated results from clinical trials may be delayed. These and other risks and uncertainties are described more fully in the section titled “Risk Factors” in Annovis Bio’s Annual Report on Form 10-K for the year ended December 31, 2021 and other periodic reports filed with the Securities and Exchange Commission. You are cautioned not to place undue reliance upon any forward-looking statements, which speak only as of the date made. Although it may voluntarily do so, from time to time, Annovis Bio undertakes no commitment to update or revise the forward-looking statements contained in this presentation, whether as a result of new information, future events or otherwise, except as required under applicable law.

COMPANY HIGHLIGHTS

Therapeutic focus/approach: treatment of Alzheimer's disease (AD) and Parkinson's disease (PD) as neurodegenerative, axonal transport diseases

Buntanetap (lead asset): only drug to improve cognition in AD **AND** motor function in PD patients

Unique MoA: restores health of nerve cells and improves function by inhibiting production of multiple neurotoxic proteins associated with AD/PD

Late-stage opportunities: Phase 3 trial in early PD patients started Aug 2022 and Phase 2/3 trial in AD started in January 2023

Proven execution: company senior leadership has consistently delivered on clinical timelines, enrollment progression, and data readouts

INVESTMENT HIGHLIGHTS

Targeting growing indications

- Parkinson's Disease – 1.2 million patients in US
- Alzheimer's Disease – 6 million patients in US

Multiple Catalysts

Key clinical and regulatory milestones

- PD – phase 3, interim data expected Q2 2023
- AD – first patient dosed in phase 2/3 trial Jan. 2023

Long Duration IP Estate IP extends well into 2030's

- Buntanetap – Multiple Methods of use for neurodegenerative diseases
- ANVS405 – Methods of use for acute brain and nerve injuries

Capital-efficient approach

- Completed \$ 50 mil. equity raise in May 2021
- Cash balance \$ 32 mil. Debt \$ 0 as of 9/30/22

PIPELINE





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

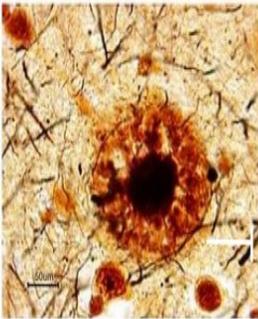
**LOSS OF COGNITIVE AND
MOTOR FUNCTION**

ANNOVIS' NEW APPROACH TO ATTACK AD AND PD

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

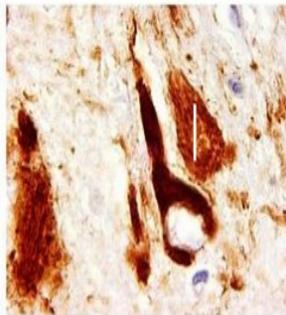
Amyloid β

Alzheimer's - Parkinson's



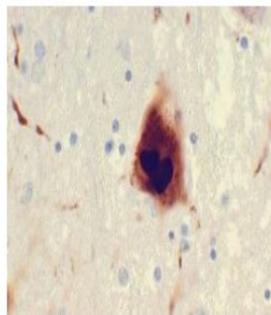
Tau

Tauopathies - AD,
PD, FTD, CTE



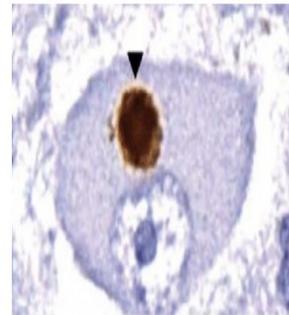
α Synuclein

Parkinson's - Alzheimer's



TDP43

ALS, AD, PD, FTD, CTE

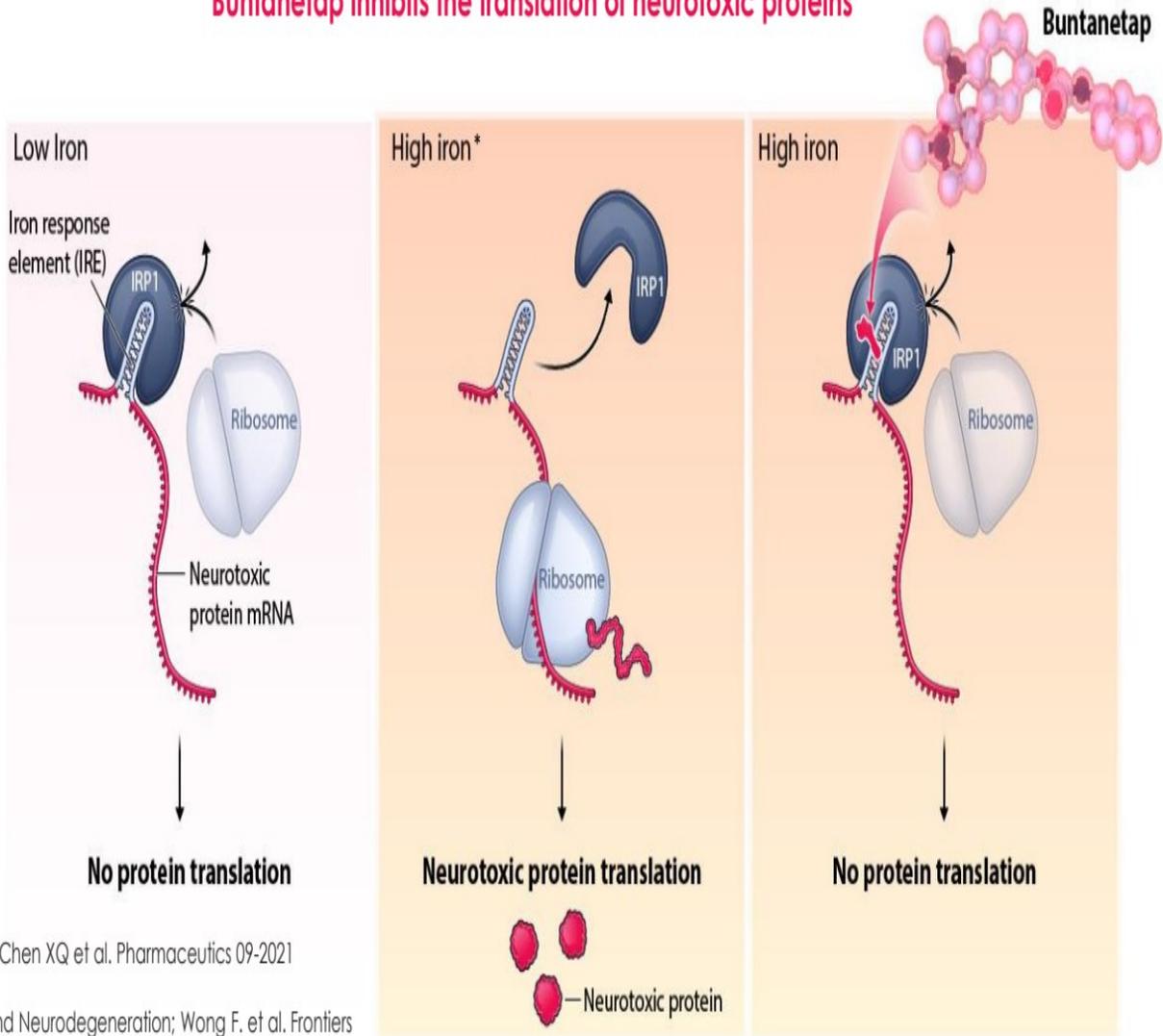


Attacking one neurotoxic protein results in minimal effect

Buntanetap inhibits the production of multiple neurotoxic proteins simultaneously

MECHANISM OF ACTION

Buntanetap inhibits the translation of neurotoxic proteins

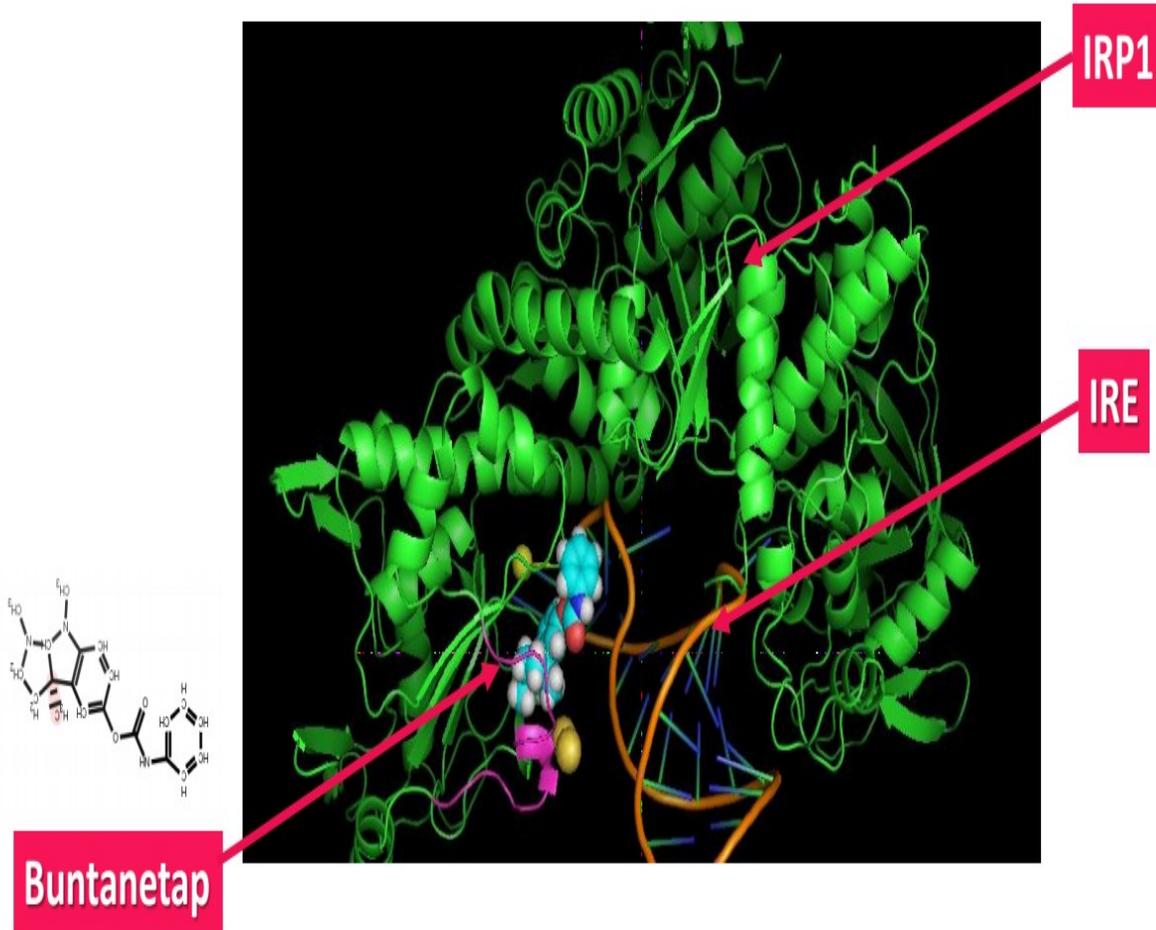


MOA; Chen XQ et al. *Pharmaceutics* 09-2021

Iron and Neurodegeneration; Wong F. et al. *Frontiers Aging Neuroscience*; 03-2022

MECHANISM OF ACTION

Molecular Model of how Buntanetap locks IRP1 in the mRNA Binding Position



Eric Baldwin, NCI

ANNOVIS 9

NEURODEGENERATION IS AN AXONAL TRANSPORT DISEASE

“Axonal transport disruption is linked to human neurological conditions.”

- Nature Review, September 2019

Axonal transport is responsible for:

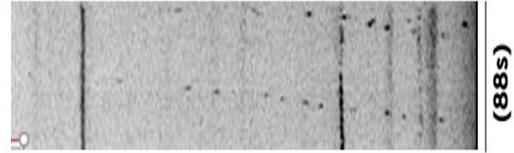
- Neurotransmitters GABA (anxiety), ACh (cognition), dopamine (movement), serotonin (mood)
- Neurotrophic factors NGF, BDNF
- All communication within and between nerve cells

Chen XQ et al. *Alzheimer's & Dementia*; 08-2020

← Retrograde (0.5 frame/sec) →

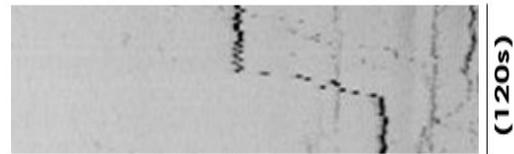
Normal Transport

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.



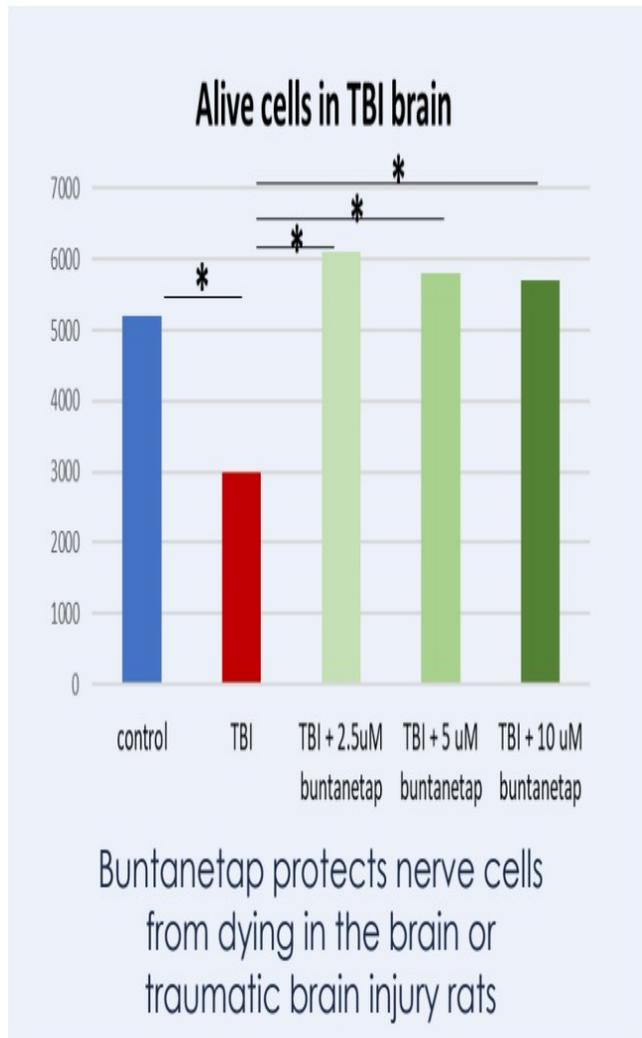
TREATED WITH BUNTANETAP

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

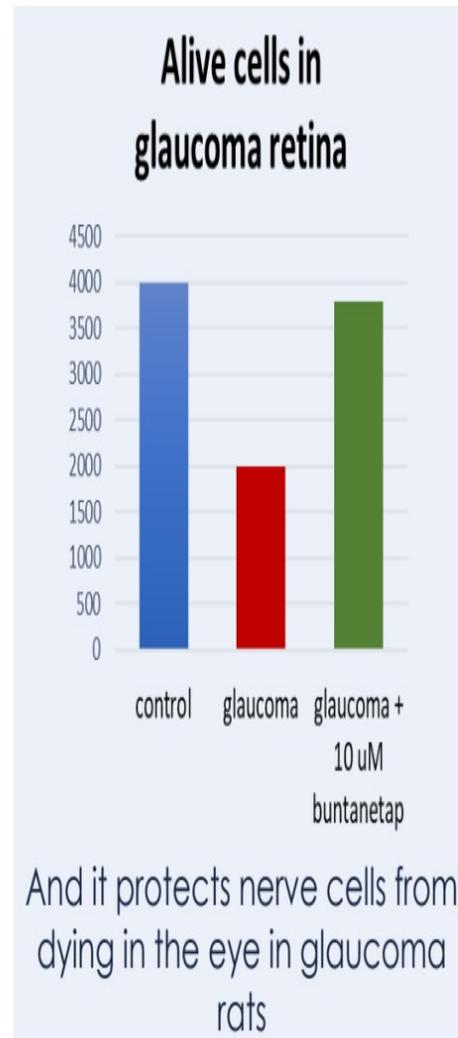


APP, Ab42, C99 – Mobley, UCSD; aSYN – Isacson, Harvard; Lee, U.Penn;
Tau – U. Muenich & Zuerich; Htt – Mobley, UCSD; TDP43 – Taylor, Northwestern

NEURODEGENERATION MEANS DEAD NERVE CELLS



Hatami A. et al: Buntanetap improves dopaminergic neuropathology and working memory in a rat model of traumatic brain injury; in preparation -UCLA



Sundstrom J. et al. Hershey Medical Center

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

BY LOWERING LEVELS OF NEUROTOXIC PROTEINS

IMPROVED AXONAL TRANSPORT

INCREASED SYNAPTIC TRANSMISSION

NO INFLAMMATION

HEALTHY NERVE CELLS

IMPROVED COGNITIVE AND MOTOR FUNCTION



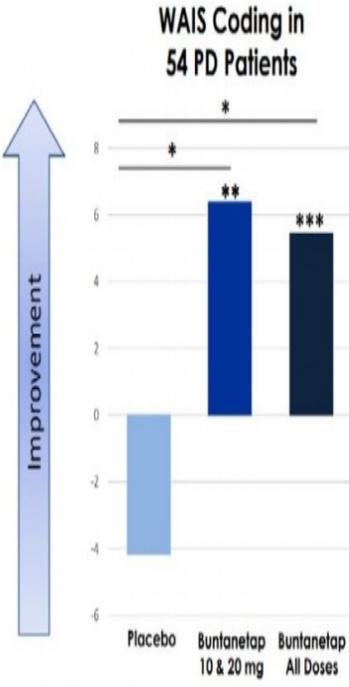
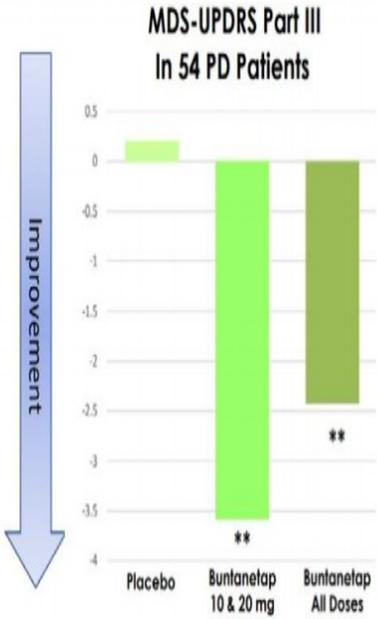
STUDIES IN EIGHT ANIMAL AND HUMAN MODELS

FUNCTION	TEST	SUBJECT
ANIMALS		
Memory, learning	Mazes	AD mice, DS mice, stroke mice, TBI rats
Movement	Colonic motility, grip strength	PD mice, tau mice
Vision	Sight	Glaucoma rats
Infections	Cell death	P. Gingivalis mice, Covid mice
HUMANS		
Cognition, memory, learning	ADAScog11 *	Early AD patients
Attention, thinking speed	WAIS coding **	Early AD patients
Movement, coordination	MDS-UPDRS ***	Early PD patients
Movement speed	WAIS coding ****	Early PD patients

BUNTANETAP PHASE 2 POSITIVE DATA IN PARKINSON'S DISEASE
SIGNIFICANT IMPROVEMENTS IN BOTH MOTOR FUNCTION AND CODING SPEED

Motor Function Improves...

.... & Coding Speed



Fang et al: Buntanetap Proves Promising in Both Alzheimer's and Parkinson's Patients; J Prevention Alzheimer Disease 10-2022

BUNTANETAP PHASE 2 POSITIVE DATA IN ALZHEIMER'S DISEASE

SIGNIFICANT IMPROVEMENTS IN BOTH COGNITIVE FUNCTION AND CODING SPEED



Fang et al: Buntanetap Proves Promising in Both Alzheimer's and Parkinson's Patients; J Prevention Alzheimer Disease 10-2022

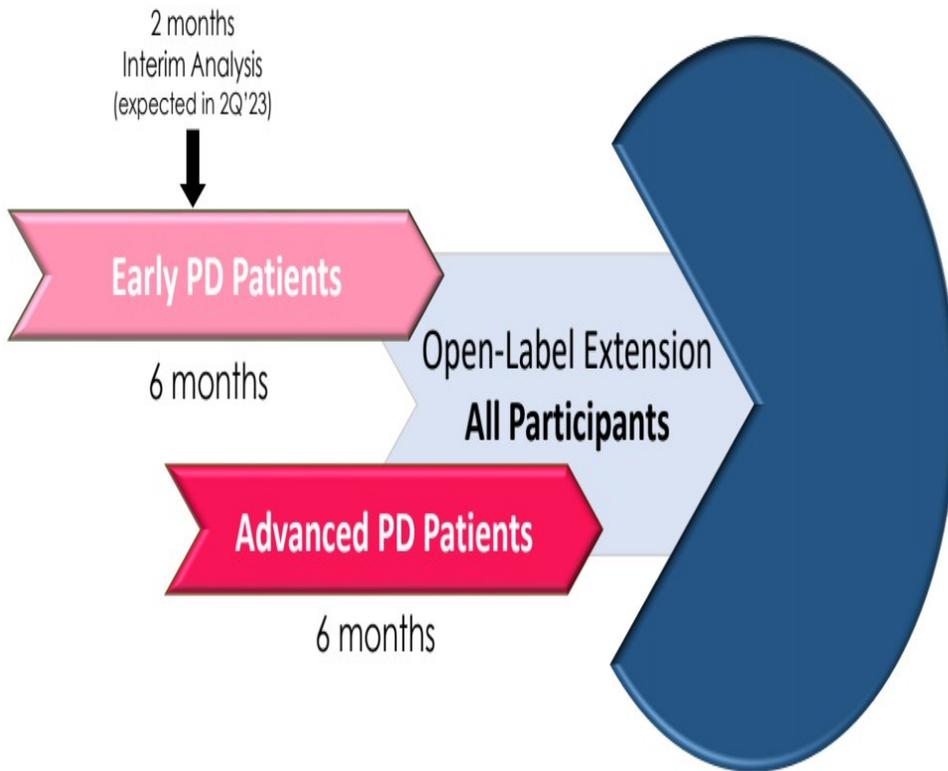
ONGOING PHASE 3 CLINICAL TRIAL IN **EARLY PD PATIENTS**

Therapeutic Area	Early PD
Phase	3
Sites	60 US + 40 EU = 100
Patients	3 X 150 = 450
Dose	0 , 10 and 20 mg/day
Start	August 2022
Design	Double-Blind, Placebo-Controlled Efficacy
Endpoints	MDS-UPDRS 2 and 3
Other	Total UPDRS, PGIC, CGIS, WAIS, Biomarkers

NCT04524351 at [ClinicalTrials.gov](https://clinicaltrials.gov).



DEVELOPMENT OF BUNTANETAP FOR **EARLY AND ADVANCED PD TO NDA**



PLANNED PHASE 2/3 CLINICAL TRIAL IN **AD PATIENTS**

Therapeutic Area	Moderate AD
Phase	2/3
Sites	80 US
Patients	4 X 80 = 320
Dose	0 , 7.5, 15 and 30 mg/day
Start	January 2023
Design	Double-Blind, Placebo-Controlled Efficacy
Endpoints	ADAScog 11, ADCS-CGIC
Other	WAIS, Biomarkers

CLINICAL DEVELOPMENT PLANS FOR **ALZHEIMER'S DISEASE**

Symptomatic Study

6 weeks
Interim Analysis
(expected in 3Q'23)



3 months

One 3-month study in moderate AD patients

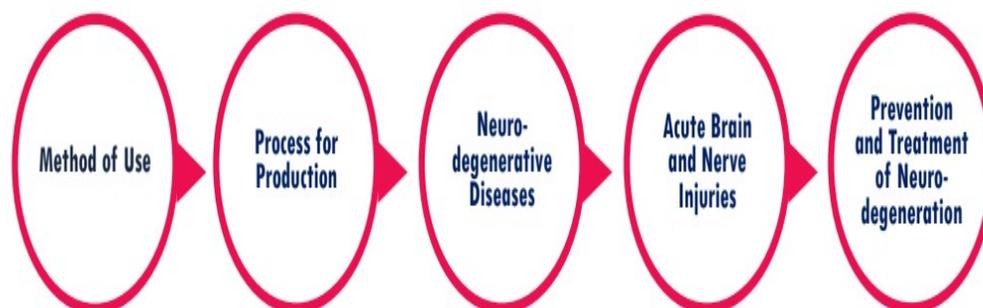
End of phase 2 study meeting with FDA to discuss full development for disease-modifying studies

Disease-modifying Study

Long chronic study in early AD

18 months

CORPORATE PATENT ESTATE



Patent/Application	Subject Matter	Status	Expiry
Provisional	Combinations	Pending	2043
Provisional	Neuropsychiatric Indications	Pending	2043
Provisional	Other Diseases	Pending	2042
PCT	Brain infections	Pending	2042
PCT	Use of mechanism of action	One patent granted	2038
PCT	Acute neurodegenerative injuries	Multiple patents granted	2036
PCT	Chronic neurodegenerative diseases	Multiple patents granted	2031

SENIOR MANAGEMENT TEAM



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

- Founded Annovis May 2008 to develop better therapeutics for neurodegeneration
- Founder and CEO of Symphony Pharmaceuticals/Annovis, a biotech company that sold in 2001 to Transgenomic
- GM of Bachem Bioscience, the US subsidiary of Bachem AG, Switzerland
- Postdocs at Caltech and Roche Institute
- PhD in biochemistry, Biocenter of Basel
- Two-year visiting fellowship at The Rockefeller University



Henry Hagopian, MBA
Chief Financial Officer

- Over 30 years in corporate finance, accounting, treasury, capital raising in public/private companies
- Former, Sr. Vice President, Finance and Treasurer at Organogenesis.
- Assisted in raising several rounds of capital at ORGO in excess of \$ 310 million.
- 15 years in AT&T, Lucent, Circor Int'l
- MBA, MS, Boston College



Cheng Fang, PhD
**SVP, Research &
Development**

- Broad scientific knowledge and over a decade in neurodegenerative diseases
- Prior experiences, Clarivate Analytics, Coriell Institute for Medical Research
- Assistant Professor, Boston University, designed projects on prion disease and AD
- Ph.D. biology/neuroscience, Penn State
- BS, Biopharmaceutics, Nanjing University



Eve Damiano, MS, RAC
SVP, Regulatory

- Over 35 years in the biotechnology sector, focusing on the definition and execution of regulatory strategies
- Has held various senior management positions at companies including Centocor, MedImmune, OraSure Technologies and Vicuron Pharmaceuticals
- track record in the definition and execution of regulatory strategies,
- MS, Drexel University College of Medicine



Melissa Gaines,
VP, Clinical Operations

- Accomplished clinical research professional with over 20 years' experience in academia, CROs and pharmaceutical companies
- Previously, Sr. Director, Clinical Operations for Worldwide Clinical Trials
- Over a decade of experience at INC Research
- Demonstrated proven success in leading cross-functional teams as well as driving operational success
- BA, Psychology Millersville University

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.



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.

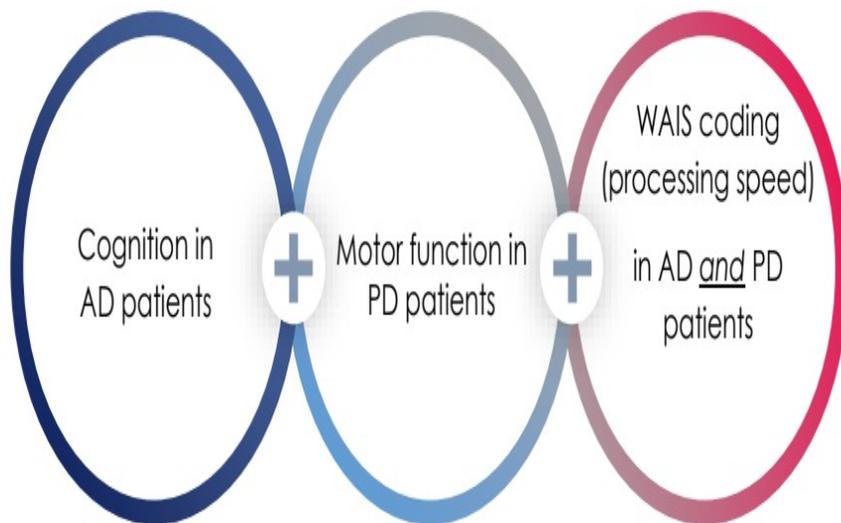


KEY TAKEAWAYS

Annovis has a novel approach to address **AD and PD**

The first double-blind, placebo-controlled study that shows improvements in **AD** patients as measured by **ADAS-Cog** and in **PD** patients as measured by **UPDRS**

Buntanetap shows improvements in **Phase 2a** clinical trials:



We started our phase 3 study for early PD, and our phase 2/3 in moderate AD



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

Symbol: **ANVS** (NYSE)

CONTACT US

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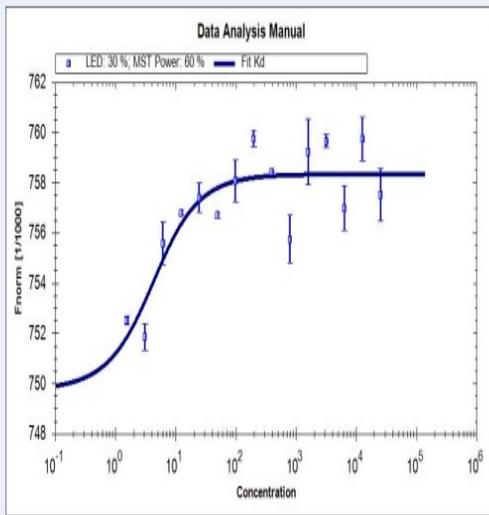
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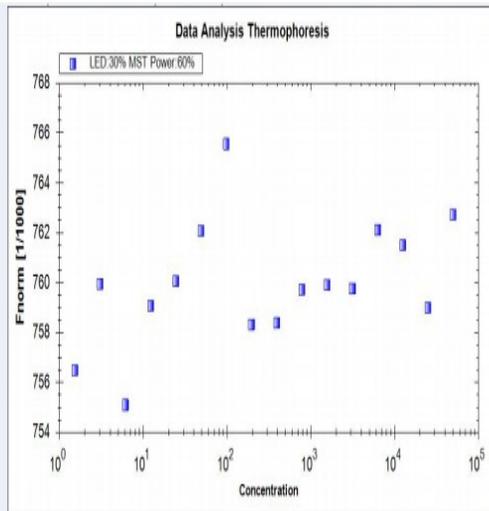
Appendix

IRE to IRP1 BINDING IS **SPECIFIC FOR** mRNAs CODING FOR **NEUROTOXIC PROTEINS**



APP IRE/IRP1/Buntanetap
Kd 3.2 nM

Fitting for Kd Formular	Fitted Value
Fitted Parameter	3.22+/-0.464
Dissociation Constant	2
Fluo.Conc	758.35
Bound	749.76
Unbound	749.76
Amplitude	8.59

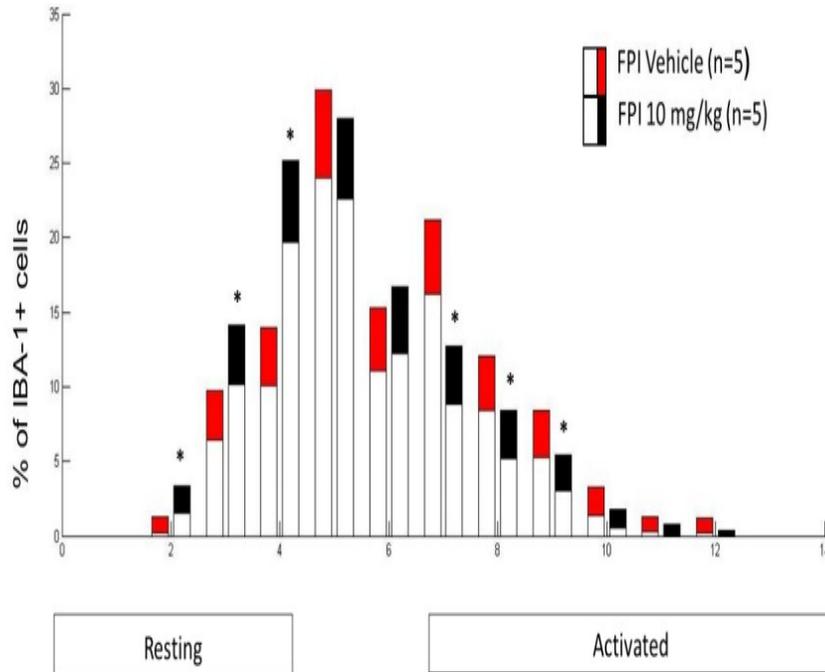


Ferritin IRE/IRP1/Buntanetap
No Kd

Buntanetap binds specifically to the APP IRE, but not to the ferritin IRE

INHIBITS MICROGLIA ACTIVATION IN RAT BRAIN

Data (Mean + 95% CI) analyzed with Bootstrapping method, *p<0.05



Microglial Cell Diameter (µm)

ANVS401 increases the number of resting microglia and reduces the number of activated microglia – it reduces inflammation