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): June 11, 2024

ANNOVIS BIO, INC.
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-39202**	**26-2540421**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

101 Lindenwood Drive, Suite 225
Malvern, PA 19355
(Address of Principal Executive Offices, and Zip Code)

(484) 875-3192
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 7.01 Regulation FD Disclosure

Annovis Bio, Inc. (“The Company”) issued a press release on June 11, 2024, outlining that its lead drug candidate, Buntanetap, showed statistically significant efficacy and safety in both carriers and non-carriers of Apolipoprotein E4 (“APOE4”), a genetic cause of Alzheimer's disease (“AD”). The press release is furnished as Exhibit 99.1 hereto.

Additionally, the Company held a webcast after market close on June 11, 2024, to discuss these findings in detail and outline future development plans for Buntanetap. A copy of the presentation materials is furnished as Exhibit 99.2 hereto.

Item 9.01 Financial Statements and Exhibits.

The following exhibits are being furnished herewith:

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release Dated June 11, 2024
99.2	Annovis Bio, Inc. – AD Webcast Presentation
104	Cover Page Interactive Data File

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: June 11, 2024

By: /s/ Maria Maccecchini
Name: Maria Maccecchini
Title: President and Chief Executive Officer

Exhibit 99.1

Annovis Bio's Buntanetap Found Safe and Effective in High-Risk Alzheimer's Patients

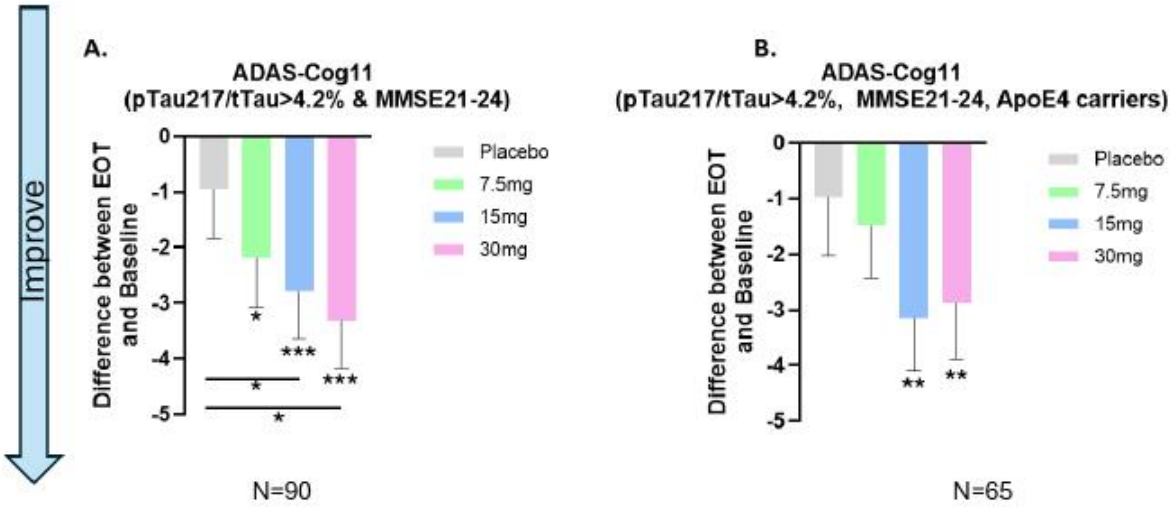
Join Our Investor Call for In-Depth Findings Discussion

MALVERN, Pa., June,11 2024 (GLOBE NEWSWIRE) -- Annovis Bio Inc. (NYSE: ANVS) ("Annovis" or the "Company"), a late-stage drug platform company developing novel therapies for neurodegenerative diseases such as Alzheimer's (AD) and Parkinson's disease (PD), today announces that its recent Phase II/III Alzheimer's study of its lead drug candidate, Buntanetap, showed statistically significant efficacy and safety in both carriers and non-carriers of Apolipoprotein E4 (APOE4), a genetic cause of AD.

Interested parties are encouraged to register for the upcoming investor call today at 4:30 PM ET, where detailed findings will be discussed.
https://zoom.us/webinar/register/3117176913600/WN_Ev_1s7l2RUKmIQJNdko5iA

Key Findings:

- **Efficacy in Early AD Patients**: In patients with early AD (MMSE 21-24), Buntanetap showed a statistically significant dose-response in ADAS-Cog11 scores, with a -3.3 points improvement over baseline and -2.3 points improvement from placebo.



- **APOE4 Carriers**: In APOE4 carriers treated with 15mg Buntanetap, there was a -3.15 improvement in ADAS-Cog11 scores.

- **Comparable Safety**: Buntanetap was found to be equally safe in both APOE4 carriers and non-carriers, with no instances of ARIA(Amyloid-Related Imaging Abnormalities).

	Placebo	7.5mg Buntanetap	15mg Buntanetap	30mg Buntanetap	All Doses
APOE Carriers (N=159)	38	45	38	38	121
# TEAEs	13(34.2%)	22(48.9%)	17(44.7%)	12(31.6%)	51(42%)
# TEAEs Related to Study Drug	1(2.6%)	8(17.8%)	6(15.8%)	3(7.9%)	17(14%)
# Serious TEAEs	3(7.9%)	0	0	1(2.6%)	1(2.5%)
# Serious TEAEs Related to Study Drug	0	0	0	0	0
APOE Non-Carriers (N=159)	41	34	43	41	118
# TEAEs	9(22.0%)	4(11.8%)	11(25.6%)	17(41.5%)	32(27.1%)
# TEAEs Related to Study Drug	1(2.9%)	1(2.9%)	2(4.7%)	3(7.3%)	6(5.1%)
# Serious TEAEs	0	0	0	2(4.9%)	2(1.7%)
# Serious TEAEs Related to Study Drug	0	0	0	0	0

- **Patient Breakdown**: The study included 159 APOE4 carriers (33 homozygotes and 126 heterozygotes) and 159 APOE4 non-carriers.

Scientific Context: Recent findings published in Nature Medicine have redefined APOE4 homozygosity as a distinct genetic form of Alzheimer's disease, requiring individualized prevention strategies, clinical trials, and treatments. This study emphasized the near-full penetrance of AD biology in APOE4 homozygotes, suggesting that these patients represent a significant target group for therapeutic interventions.

Safety Insights:

Safety Insights: Dr. Samuel Gandy, an Alzheimer's researcher at Mount Sinai, highlighted the heightened safety risks for APOE4 homozygotes from anti-amyloid drugs, such as Leqembi, which have been associated with serious side effects like brain swelling and bleeding. When the Food and Drug Administration approved the anti-amyloid drug Leqembi last year, it required a black-box warning — the agency's strongest caution — because of safety concerns for people with two copies of APOE4. However, Buntanetap demonstrated no increased safety issues compared to placebo, even in APOE4 carriers.

During our upcoming investor call, we will discuss the recent New York Times article that underscores the serious implications for APOE4 carriers.

Future Plans: Encouraged by these results, Annovis Bio is planning an 18-month Phase III trial focusing on biomarker-positive early AD patients. This trial aims to further validate Buntanetap's efficacy and safety profile and will be conducted under the guidance of the FDA.

Investor Call: Annovis Bio will host an investor call to discuss these findings in detail and outline the future development plans for Buntanetap.

- **Date and Time:** June 11, 2024, 4:30pm ET.
- **Register Now:** https://zoom.us/webinar/register/3117176913600/WN_Ev_1s7l2RUKmIQJNdko5iA

About Buntanetap: Buntanetap (formerly known as Posiphen or ANVS401) targets neurodegeneration by inhibiting the formation of multiple neurotoxic proteins, including amyloid beta, tau, alpha-synuclein, and TDP43. By improving synaptic transmission, axonal transport, and reducing neuroinflammation, Buntanetap aims to reverse neurodegeneration in AD, PD, and other neurodegenerative diseases.

About Annovis Bio Inc.: Headquartered in Malvern, Pennsylvania, Annovis Bio Inc. is dedicated to addressing neurodegeneration in diseases such as AD and PD. The company's innovative approach targets multiple neurotoxic proteins, aiming to restore brain function and improve the quality of life for patients. For more information, visit www.annovisbio.com and follow us on LinkedIn and X .

Forward-Looking Statements

This press release contains "forward-looking" statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements include, but are not limited to, the Company's plans related to clinical trials. Forward-looking statements are based on current expectations and assumptions and are subject to risks and uncertainties that could cause actual results to differ materially from those projected. Such risks and uncertainties include, but are not limited to, those related to patient enrollment, the effectiveness of Buntanetap, and the timing, effectiveness, and anticipated results of the Company's clinical trials evaluating the efficacy, safety, and tolerability of Buntanetap. Additional risk factors are detailed in the Company's periodic filings with the SEC, including those listed in the "Risk Factors" section of the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q. All forward-looking statements in this press release are based on information available to the Company as of the date of this release. The Company expressly disclaims any obligation to update or revise its forward-looking statements, whether as a result of new information, future events, or otherwise, except as required by law.

Contacts

Annovis Bio, Inc.
101 Lindenwood Drive
Suite 225
Malvern, PA 19355
www.annovisbio.com

Investor Contact

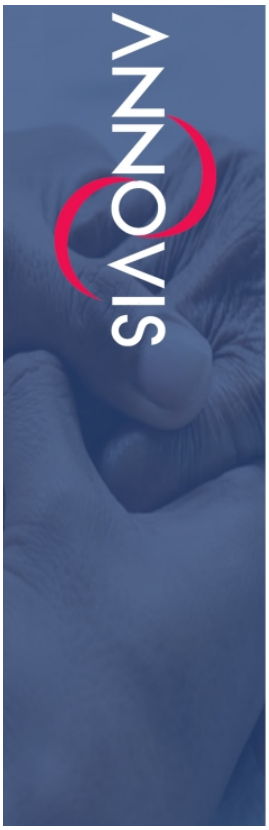
Scott McGowan
InvestorBrandNetwork (IBN)
Phone: 310.299.1717
IR@annovisbio.com
Investor Website

Exhibit 99.2


ANNOVIS
- People Focused, Purpose Driven, Passion Powered -
Investor Webcast
6/11/2024
NYSE: ANVS

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, 2022, 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.



Today's Presentation

- Study design
- Primary endpoint results in ITT population
- Subgroup analysis based on biomarker and MMSE scores
- ADAScog11 in early AD patients
- Subgroup analysis based on APOE status
- ADAScog11 in APOE4 carriers/non-carriers
- Safety in early AD patients, APOE4 carriers/non-carriers

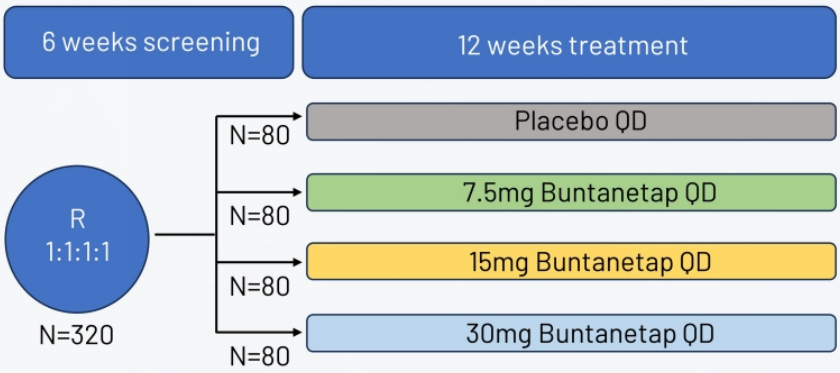
RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING, MULTICENTER STUDY IN MILD TO MODERATE ALZHEIMER'S PATIENTS

Key Inclusion Criteria:

- Diagnosis of AD according to NIA and NIA-AA criteria (2011)
- Age 55 to 85
- MMSE 14-24

Key Clinical Outcome:

- Primary Endpoints:
- ADAS-Cog 11
- CGIC



Key Secondary Endpoint:

- ADCS-ADL

PRIMARY ENDPOINT IN ITT POPULATION (N=351)

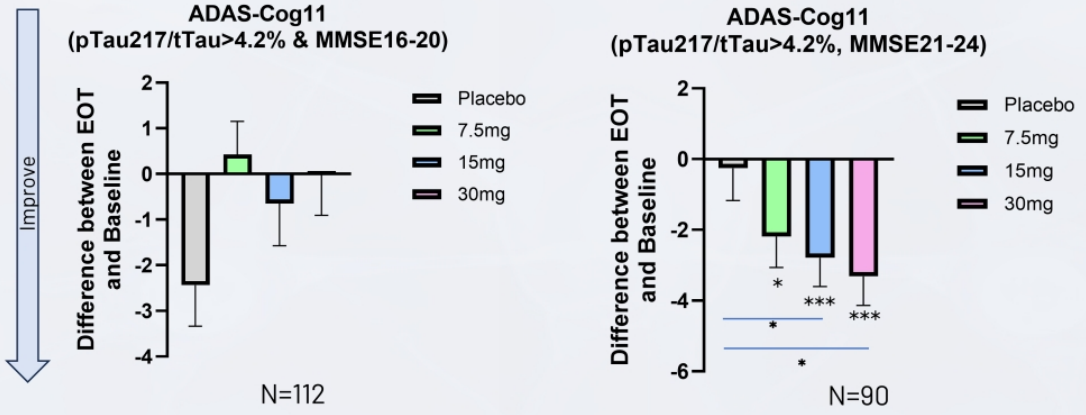
ADAS-Cog11	Placebo (N=89)	7.5mg Buntanetap (N=88)	15mg Buntanetap (N=87)	30mg Buntanetap (N=87)
Baseline				
N	85	86	87	87
Mean Score (SD)	20.28 (6.79)	23.20 (7.59)	22.74 (7.57)	21.85 (7.16)
End of Trial (12 weeks)				
N	81	82	78	79
Mean Score (SD)	18.33 (6.94)	21.42 (8.42)	19.26 (7.70)	20.21 (8.94)
Difference from Baseline	-2.182	-1.452	-2.992	-2.304
P-value	0.001	0.001	0.001	0.001
Difference from Placebo		0.98 (0.75)	-0.68 (0.76)	0.09 (0.75)
P-value		0.193	0.366	0.910

BIOMARKER BASED PATIENT STRATIFICATION (pTau217/tTau>4.2%, N=210)

MMSE 21-24 BASED PATIENT STRATIFICATION, N=90

	Placebo (N=89)	7.5mg Buntanetap (N=88)	15mg Buntanetap (N=87)	30mg Buntanetap (N=87)
ITT N	85	86	87	87
AD (pTau217/tTau>4.2%) N	51	57	51	51
AD MMSE 14-20	25	36	26	25
AD MMSE 21-24	21	20	24	25

ADAScog11 IN AD PATIENTS



Buntanetap statistically and clinically significantly improved ADAS-Cog11 in patients with mild AD

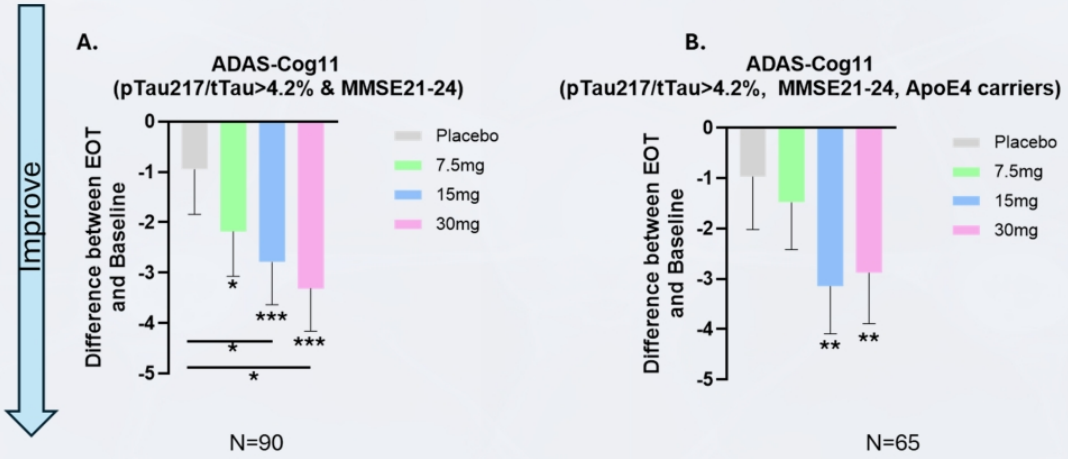
SUBGROUP ANALYSIS BASED ON APOE STATUS

EARLY AD PATIENTS N=90
APOE4 CARRIERS N=66; NON-CARRIERS N=24

	Placebo	7.5mg Buntanetap	15mg Buntanetap	30mg Buntanetap
AD (pTau217/tTau>4.2%) MMSE21-24	21	20	24	25
AD MMSE 21-24 ApoE4 carriers	16	17	15	18
AD MMSE 21-24 Non ApoE4 carriers	5	3	9	7

ADAScog11 AND APOE4 STATUS

ApoE4 carrier (+/- & +/+) 66.5% in pTau217/tTau>4.2% population
vs ApoE4 carrier 22.6% in pTau217/tTau<4.2% population



Buntanetap improves ADAS-Cog11 equally in APOE4 carriers and non-carriers

SAFE IN APOE4 CARRIERS AND NON-CARRIERS IN ITT POPULATION AND EARLY AD PATIENTS

	Placebo	7.5mg Buntanetap	15mg Buntanetap	30mg Buntanetap	All Doses
APOE Carriers (N=159)	38	45	38	38	121
# TEAEs	13 (34.2%)	22 (48.9%)	17 (44.7%)	12 (31.6%)	51 (42%)
# TEAEs Related to Study Drug	1 (2.6%)	8 (17.8%)	6 (15.8%)	3 (7.9%)	17 (14%)
# Serious TEAEs	3 (7.9%)	0	0	1 (2.6%)	1 (2.5%)
# Serious TEAEs Related to Study Drug	0	0	0	0	0
APOE Non-Carriers (N=159)	41	34	43	41	118
# TEAEs	9 (22.0%)	4 (11.8%)	11 (25.6%)	17 (41.5%)	32 (27.1%)
# TEAEs Related to Study Drug	1 (2.9%)	1 (2.9%)	2 (4.7%)	3 (7.3%)	6 (5.1%)
# Serious TEAEs	0	0	0	2 (4.9%)	2 (1.7%)
# Serious TEAEs Related to Study Drug	0	0	0	0	0

AE = Adverse Event
TEAE = Treatment Related Adverse Event

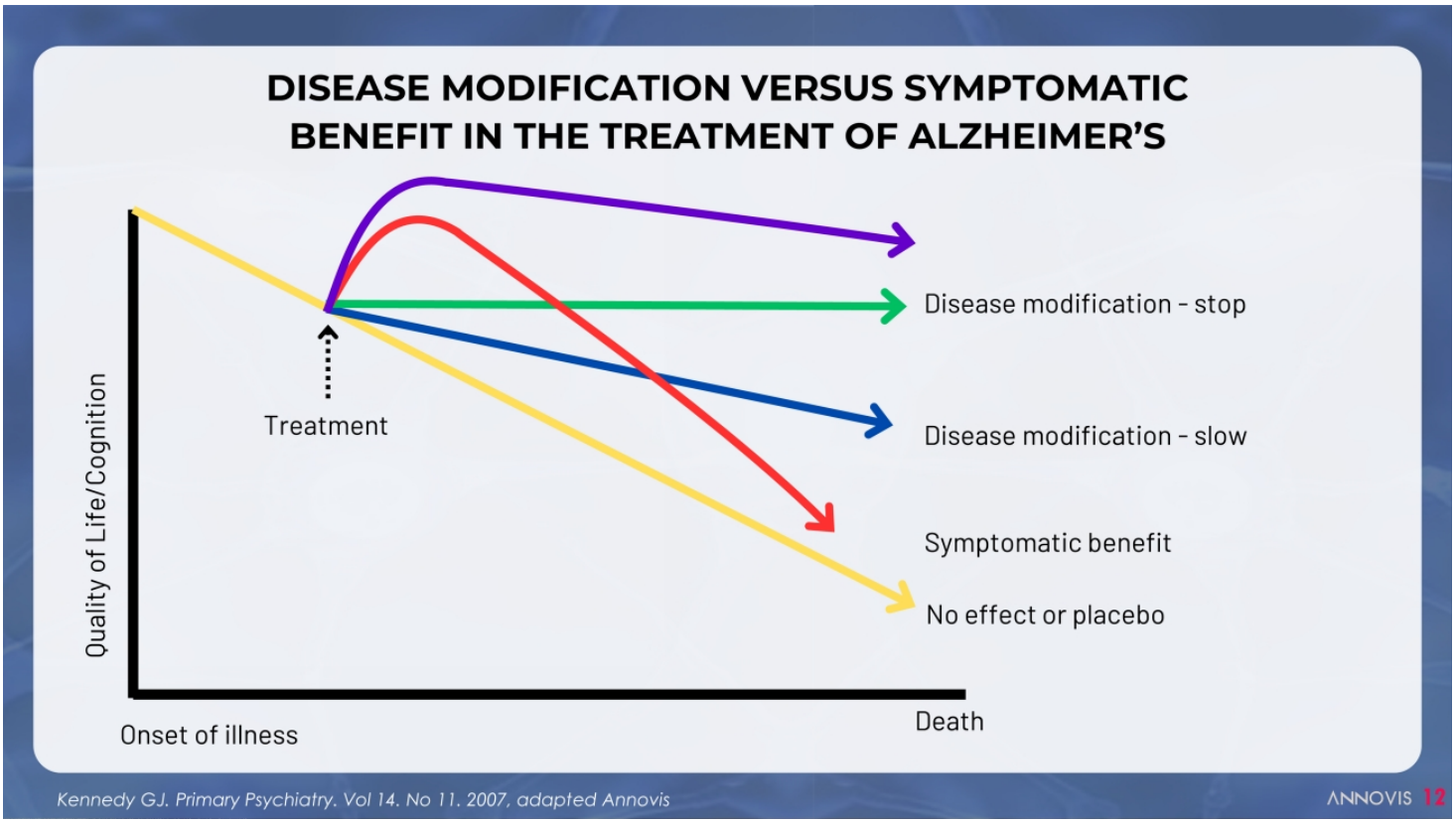
COMPARISON WITH APPROVED AD DRUGS

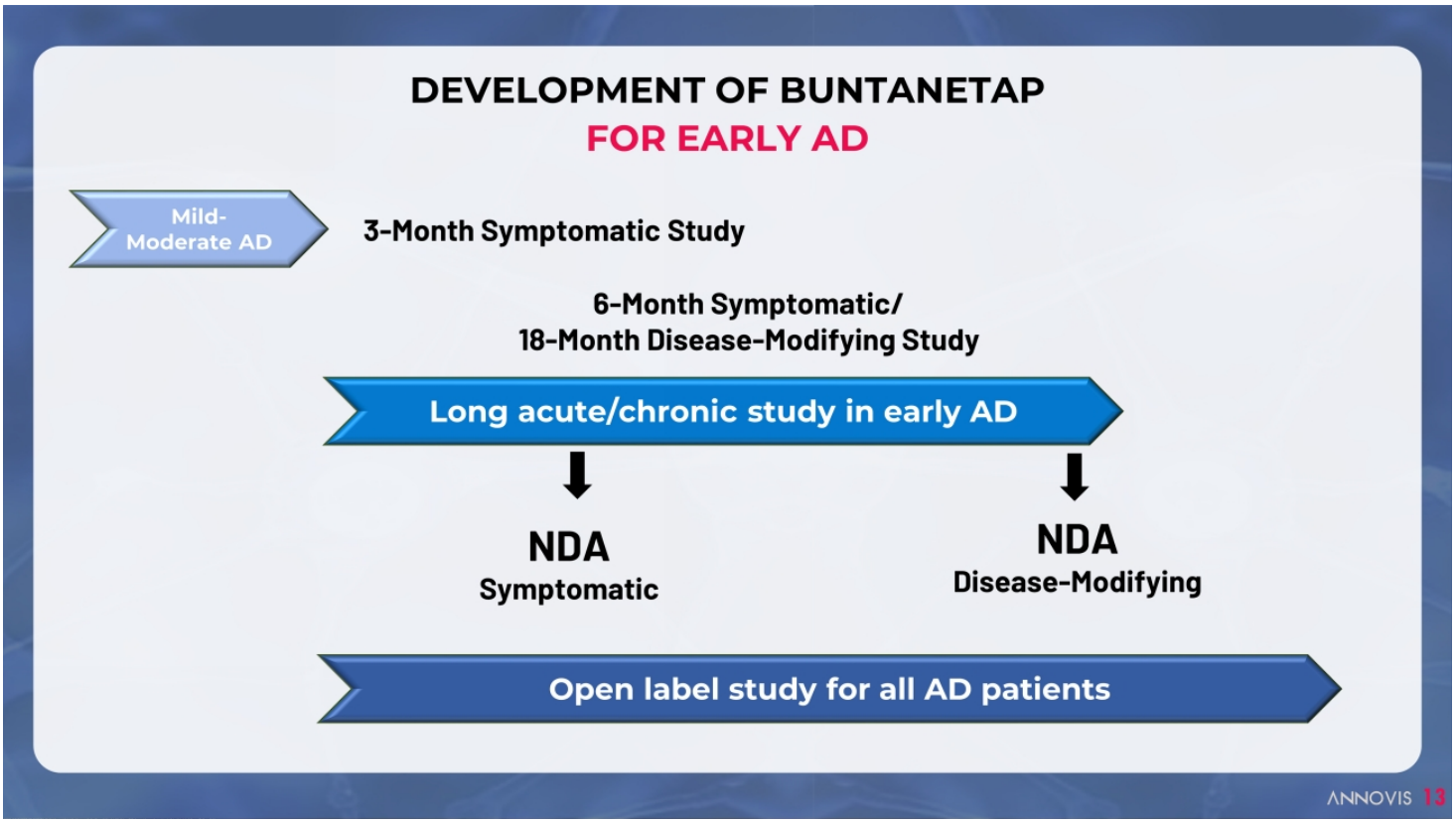
Study	Drug	AD Patient	Endpoint	Comparison 12 Weeks	Drug vs Baseline	Drug vs Placebo	Comparison End of Study	Drug vs Baseline	Drug vs Placebo
ANVS Phase IIa	Buntanetap	MMSE 18-28	ADAS-Cog11	1 month	-4.4	-3.2			
ANVS Phase II/III	Buntanetap	MMSE 21-24	ADAS-Cog11	12 weeks	-3.3	-2.36			
ANVS Phase II/III	Buntanetap	MMSE 14-20	ADAS-Cog11	12 weeks	-0.65	1.79			
Eisai	Aricept	MMSE 21-26	ADAS-Cog13	12 weeks	-1.5	-2	24 weeks	-2	-2.3
Eisai	Leqembi	MMSE 22-30	ADAS-Cog14	12 weeks	+0.5	-0.5	72 weeks	+4	-1.44
Ely Lilly	Donanemab	MMSE 22-28	ADAS-Cog13				78 weeks	+3.17	-1.52

- Aricept is a **SYMPTOMATIC** approved drug: it improves cognition by -1.5 points at 3 months and -2 points at 6 months. After that the efficacy wanes.

- Leqembi is a **DISEASE-MODIFYING** drug: it does not improve the symptoms; in fact, at 3 months there is no difference from baseline. It slows the progression of the disease. At 18 months patients on Leqembi worsen by +4 points, whereas patients on placebo worsen by +5.44 points. Leqembi slows the decline by -1.44 points.

- Buntanetap at 3 months looks like a very strong **SYMPTOMATIC** drug. A longer 18-month study will show whether it has **DISEASE-MODIFYING** effects.


DISEASE MODIFICATION VERSUS SYMPTOMATIC BENEFIT IN THE TREATMENT OF ALZHEIMER'S
Disease modification - stop
Disease modification - slow
Symptomatic benefit
No effect or placebo
Treatment
Quality of Life/Cognition
Onset of illness
Death
Kennedy GJ. Primary Psychiatry. Vol 14. No 11. 2007, adapted Annovis
ANNOVIS 12


DEVELOPMENT OF BUNTANETAP
FOR EARLY AD
Mild-
Moderate AD
3-Month Symptomatic Study
6-Month Symptomatic/
18-Month Disease-Modifying Study
Long acute/chronic study in early AD
NDA
Symptomatic
NDA
Disease-Modifying
Open label study for all AD patients
ANNOVIS 13


ANNOVIS
CONTACT US
101 Lindenwood Drive
Malvern, PA 19355
ir@annovisbio.com
www.annovisbio.com
Q&A Session
NYSE: ANVS
ANNOVIS 14


ANNOVIS
CONTACT US
101 Lindenwood Drive
Malvern, PA 19355
ir@annovisbio.com
www.annovisbio.com
Thank You for Your Support
NYSE: ANVS
ANNOVIS 15