2019 ALZHEIMER'S DRUG PIPELINE THE CURRENT STATE OF ALZHEIMER'S DRUG DEVELOPMENT

PHASE 3 FACTS 2019	Percent Change from 2018
Number of Drugs: 26	↓ -16%
Commercial Launch: 22 drugs could reach the market in the next f	ive years 🕹 -12%
Number of Symptomatic Drugs: 9	↓ -25%
Number of Disease Modifying Drugs: 17	↓ -11%
Prevention Trials: 6 drugs are in prevention t	trials 🕹 -14%
Mechanism of Action: 7 drugs classified as Amyloid 12 drugs classified as Neurotransmission	 ↓ -30% ↓ -14%

PHASE 2 FACTS 2019 Percent Change from 2018 Number of Drugs: 72 **1**06% **Commercial Launch:** 7 drugs could reach the market in the next five years **↓**-13% Number of Symptomatic Drugs: 13 00% Number of Disease Modifying Drugs: 59 **1** 07% Prevention Trials: 2 drugs are in prevention trials 00% Mechanism of Action: 5 drugs classified as Neuronal + Synaptic Growth **1** 67% **1** 09% 12 drugs classified as Tau

A Breakdown by Mechanism of Action



Symptomatic vs. Disease-Modifying

A Disease-Modifying drug is one that attempts to alter the underlying pathobiology of Alzheimer's disease and is being tested with biomarkers.

A Symptomatic drug is one that attempts to lessen the symptomology often associated with Alzheimer's disease, such as agitation, aggression, and insomnia.

Prevention Trials

Prevention trials are all trials conducted on pre-symptomatic participants, including those who are healthy and cognitively normal.

Methodology

This analysis was constructed through extensive research and interviews, including interviews with company executives about publicly available information, SEC filings, company reports, presentations at medical conferences, and media coverage. Additionally, academic research experts and select RA2 members provided input and review of the analysis. However, the responsibility for the content of this report belongs solely to UsAgainstAlzheimer's, the convener of RA2, and not to any other organization or individual. Information presented in this analysis includes Alzheimer's drugs that are in Phase 2 and Phase 3. This information is subject to change given the nature of clinical trials and drug development. Our intention is to provide regular updates on the status of drug development in Alzheimer's, and we welcome input and corrections. Contact: dholzapfel@highlanterrgroup.com

ResearchersAgainst Alzheimer's



PHASE 3 Alzheimer's Drugs and Estimated Commercial Launch Dates

		2018	2019	2020	2021	2022	2023	2024	2025	2026	2027
A	Sodium Oligo-mannurarate ¹ Shanghai Greenvalley Pharmaceutical Co.										
\mathbb{N}	Zolpidem Brasilia University Hospital										
(\mathbb{N})	Zoplicone Brasilia University Hospital										
N	AXS-05 Axsome Therapeutics, Inc.										
0	Docosahexaenoic acid ² University of Southern California; Alzheimer's Association										
1	Masitinib AB Science										
\mathbb{N}	AVP-786 Avanir Pharmaceuticals										
\mathbb{N}	Donepezil Transdermal Patch Icure Pharmaceutical Inc.										
\mathbb{N}	Troriluzole Biohaven Pharmaceuticals, Inc.										
(\mathbb{N})	Octohydroaminoacridine Succinate Shanghai Mental Health Center										
(\mathbb{N})	Methylphenidate National Institute on Aging;										
0	Johns Hopkins Bloomberg School of Public Health ALZT-OP1³ AZTherapies										
(Ī)	TRx0237 TauRx Therapeutics										
(\mathbb{N})	Brexpiprazole Otsuka Pharmaceuticals										
(\mathbb{N})	Guanfacine Imperial College London										
0	ANAVEX 2-73 ⁴ Anavex Life Sciences Corp.										
0	Icosapent Ethyl VA Office of Research and Development;										
A	University of Wisconsin, Madison Solanezumab Eli Lilly										
\mathbb{N}	Escitalopram JHSPH Center for Clinical Trials; National Institute on Aging										
\mathbb{N}	AGB101 AgeneBio, Inc.; National Institute on Aging										
(a)	COR388 HCI Cortexyme Inc.										
A	Gantenerumab Roche / Genentech (In-licensed from Morphosys)										
A	E2609 Eisai Co., Ltd. and Biogen										
A	BAN2401 Eisai Co., Ltd. and Biogen										
A	CAD106 Novartis Pharmaceuticals										
A	CNP520 Novartis Pharmaceuticals	2018	2010	2020	2021	2022	2023	20.24	2025	2026	2027

KEY 📕 Estimated Trial Completion 📕 Estimated Regulatory Filing 📕 Estimated Commercial Launch Date

MOA (A) Amyloid (B) Blood + Vascular (C) Stem Cell (1) Inflammation (1) Inflammation (1) Inflammation (1) Inflammation (1) Inflammation (2) Antimicrobial

PHASE 2 Alzheimer's Drugs and Estimated Commercial Launch Dates



KEY Estimated Trial Completion Estimated Regulatory Filing Estimated Commercial Launch Date

MOA 🕼 Amyloid 🚱 Blood + Vascular 🛈 Stem Cell 🕕 Inflammation 🕞 Insulin + Glucose 🚯 Neurotransmission 🚱 Neuronal + Synaptic Growth 🕕 Other 🕤 Tau 🔅 Endocrine @ Antimicrobial

(R+)	Telmicartan	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029
U	Sunnybrook Health Sciences Centre												
0	LM11A-31-BHS PharmatrophiX Inc.; National Institute on Aging												
0	UCMSCs South China Research Center for Stem Cell and												
0	iversity of Kansas Medical Center; Ausio Pharmaceuticals												
\mathbb{N}	BI 425809 Boehringer Ingelheim												
0 Chars	BAC re Biotechnology Corp.; A2 Healthcare Taiwan Corporation												
0	Benfotiamine Burke Medical Research Institute												
0	GRF6019 Alkahest, Inc.												
(†)	Liraglutide Imperial College London												
0	Curcumin VA Office of Research and Development; Verdure Sciences												
\mathbb{N}	DAOI Chang Gung Memorial Hospital												
0	Posiphen QR Pharma Inc.												
A	GB301												
A	Nilotinib Georgetown University												
Ţ	IONIS-MAPTRx Ionis Pharmaceuticals, Inc.												
\mathbb{N}^+	CERE-110 Sangamo Therapeutics												
0	MMFS-205-SR Neurocentria, Inc; Ohio State University												
A	ALZ-801 ⁵												
	Sargramostim Genzyme, Sanofi, University of Colorado Denver												
0	Allogeneic Human Mesenchymal Stem Cells Stemedica Cell Technologies, Inc.												
0	BPN14770 Tetra Discovery Partners												
T	Nicotinamide												
(Ī)	R07105705												
(0)	Roche / Genentech (In-licensed from AC Immune)												
	Neuroscience Trials Australia	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029

KEY 📕 Estimated Trial Completion 📕 Estimated Regulatory Filing 📕 Estimated Commercial Launch Date

MOA (A) Amyloid (B) Blood + Vascular (C) Stem Cell (1) Inflammation (b) Insulin + Glucose (N) Neurotransmission (b) Neuronal + Synaptic Growth (0) Other (1) Tau (E) Endocrine (a) Antimicrobial



KEY Estimated Trial Completion Estimated Regulatory Filing Estimated Commercial Launch Date

MOA (A) Amyloid (B) Blood + Vascular (C) Stem Cell (1) Inflammation (b) Insulin + Glucose (N) Neurotransmission (b) Neuronal + Synaptic Growth (0) Other (1) Tau (E) Endocrine (a) Antimicrobial

FOOTNOTES:

- 1. All drug commercial launch dates in these charts assume trial success in Phase 3. And all commercial launch dates are estimates made by RA2 based on the formulas outlined below.
- 2. Drugs are labeled as Other when the medication's Mechanism of Action (MOA) is not clearly defined within the MOA categories RA2 uses for the purposes of this report.
- 3. We recognize this drug's mechanism of action could be classified as both Amyloid and Inflammation. For the purposes of this report, we have classified it as Other.
- 4. In some cases, a drug is currently enrolled in both Phase 2 and Phase 3 clinical trials. For these anomalies, RA2 always assumed the same Phase 3 regulatory filing and commercial launch date for both trials so that there is consistent information on when a drug may reach the market.
- 5. The trial completion date, regulatory filing and commercial launch date are based on an estimate made by RA2.

PHASE 2 + 3 COMMERCIAL LAUNCH FORMULAS:

PHASE 3:

DEFINITIONS:

For the purposes of this report, Phase 3 drugs are those in either Phase 3 or Phase 2/3 clinical trials.

PHASE 3 FORMULA:

LPV to Regulatory Filing: 6 months Regulatory Filing to Commercial Launch Date: 12 months

PHASE 2:

DEFINITIONS: For the purposes of this report, Phase 2 drugs are those in either Phase 2 or Phase 1/2 clinical trials.

PHASE 2 FORMULA (SX DRUGS):

Phase 2 LPV to Start of Phase 3 Enrollment: 12 months Phase 3 Enrollment Period + Treatment Period: 24 months + 6 months LPV to Regulatory Filing: 6 months Regulatory Filing to Commercial Launch Date: 12 months

PHASE 2 FORMULA (DM DRUGS):

Phase 2 LPV to Start of Phase 3 Enrollment: 12 months Phase 3 Enrollment Period + Treatment Period: 24 months + 24 months LPV to Regulatory Filing: 6 months Regulatory Filing to Commercial Launch Date: 12 months

AUTHORS:

Dr. David Morgan, Michigan State University Drew Holzapfel, UsAgainstAlzheimer's Patrick Rochelle, UsAgainstAlzheimer's Jeremiah Paskus, UsAgainstAlzheimer's

