Sage Therapeutics™

J.P. Morgan Healthcare Conference

January 2021

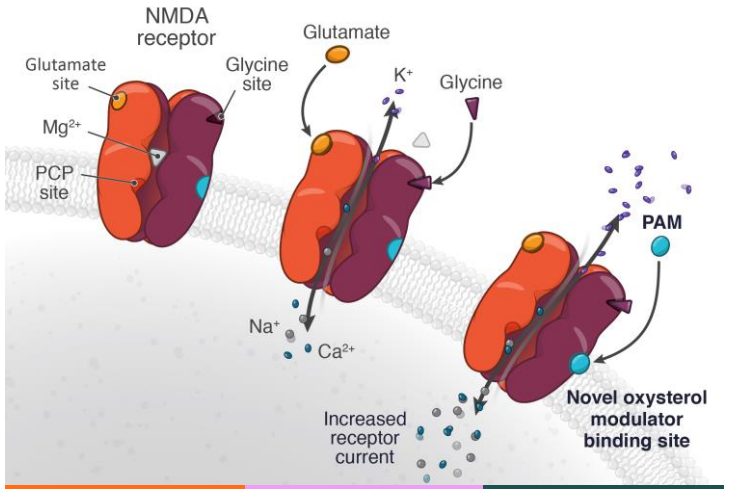
Safe Harbor Statement

- The slides presented today and the accompanying oral presentations contain forward-looking statements, which may be identified by the use of words such as “may,” “might,” “will,” “should,” “can,”,“expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “opportunity”, “goal”, “mission”, “potential,” or “continue,” and other similar expressions.
- Forward-looking statements in this presentation include statements regarding: our clinical development plans, including expected timelines for initiation and completion of trials and reporting of results; the potential regulatory pathways for our product candidates; our belief in the potential of our product candidates in various indications; the potential profile and benefit of our product candidates; our estimates as to the number of patients with disorders and diseases of interest to us; the goals, opportunity and potential for our business; our views with respect to potential value creation opportunities, including the potential benefits and results that may be achieved through our collaboration with Biogen; our plans for advancing, accelerating and expanding our development efforts and the output of our product engine; our belief in the potential for upcoming catalysts and milestones to support our mission of bringing innovative medicines to patients; and our belief in our ability to become a multi-franchise, leading brain health company.
- These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:
  - Our clinical trials may not meet their primary endpoints or key secondary endpoints. Success in non-clinical studies or in prior clinical trials of our product candidates may not be repeated or observed in ongoing, planned or future studies involving the same compound or other product candidates. Final results of studies where we reported interim results may not be consistent with the interim results. Non-clinical and clinical results from ongoing or future trials may not support further development of the product candidate or regulatory approval on the timelines we expect or at all or may require additional clinical trials or nonclinical studies.
  - We may experience slower than expected enrollment in our clinical trials or may encounter other delays or problems, including in analyzing data or requiring the need for additional analysis, data or patients, and such issues with any trial could cause delay in completion of the trial, availability of results and timing of future activities.
  - The impact of COVID-19 on our clinical development timelines may be more significant than we expect and may negatively impact expected site initiation, enrollment or conduct in our clinical trials, or cause us to pause trials or not be able to use data, in each case which may significantly impact our ability to meet our expected time-lines or may significantly impact the integrity or sufficiency of the data from our trials or cause us to have to change our plans.
  - We may encounter unexpected safety or tolerability issues with respect to any of our product candidates or marketed products; we may encounter different or more severe adverse events at the higher doses or in new indications we are studying in ongoing and planned trials; we may encounter issues with the efficacy or durability of short-term treatment, or co-initiated treatment with zuranolone or safety and efficacy concerns with respect to retreatment that require additional studies be conducted;
  - The FDA and other regulatory authorities may ultimately decide that the design or results of our completed, ongoing or planned clinical trials for any of our product candidates, even if positive, are not sufficient to file for or obtain regulatory approval in the indications that are the focus of our development plans despite prior regulatory advice. At any stage, regulatory authorities may ask for additional clinical trials, nonclinical studies or other data in order for us to proceed further in development or to file for or obtain regulatory approval, and we may not be successful in those efforts. Other decisions or actions of the FDA or other regulatory authorities may affect the initiation, timing, design, size, progress and cost of clinical trials and our ability to proceed with further development;
  - We may never achieve the rate of new product candidates from our product engine that we expect in the future.
  - Even if our products are successfully developed and approved, the number of patients with the diseases or disorders our products treat, and the actual market for such products may be smaller than our current estimates; or we may not achieve market acceptance or reimbursement at acceptable levels.
  - The anticipated benefits of our collaboration with Biogen may never be achieved
  - We may not be able to obtain and maintain adequate intellectual property protection or other forms of data and marketing exclusivity for its products, or to defend ours patent portfolio against challenges from third parties.
  - We may face competition from others developing products for similar uses as those for which our product candidates are being developed.
  - Our operating expenses may be higher than forecasted, and we may also face unexpected expenditures which could cause us to change our plans.
  - We may not be able to establish and maintain key business relationships with third parties on we may encounter technical and other unexpected hurdles in the manufacture and development of our products.
  - Any of the foregoing or other factors may negatively impact our ability to achieve our goals, mission, opportunities, plans or expectations for our business.
- For additional disclosure regarding these and other risks Sage faces, see the disclosure contained in the "Risk Factors" section of our most recent report, and in our other public filings with the Securities and Exchange Commission, available on the SEC's website at http://www.sec.gov. Any forward-looking statement represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We undertake no obligation to update or revise the information contained in this presentation, whether as a result of new information, future events or circumstances or otherwise.

Sage Therapeutics™

Sage is a leader in brain health – *making medicines that matter*

- Advancing Brain Health Leadership
- Mission to be a top-tier biopharmaceutical company in the next 5 years
- Rich pipeline across 3 franchises
  - First and only product approved specifically for postpartum depression
  - Two late-stage programs; four ongoing phase 3 studies
  - 5 NCE development programs across 9+ indications
  - Strong intellectual property strategy
- Goal of 2 or more IND-enabling programs per year by 2023
- Catalyst rich 2021; expected topline readouts from ten clinical trials
- $2B+ capital to fund efforts to accelerate and advance medicines that have potential to impact an estimated > 450M patients globally



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Brain Health Disorders — Global Healthcare Challenge

In 10 years, Sage has expanded the potential for solutions and through collaborations expects to further accelerate and expand estimated patient reach

~18M

Sage

Postpartum Depression

Major Depressive Disorder

Brain Health Disorders — Global Healthcare Challenge

In 10 years, Sage has expanded the potential for solutions and through collaborations expects to further accelerate and expand estimated patient reach

~22M

Sage + Shionogi

18M

Sage

Postpartum Depression	
Major Depressive Disorder	
	Shionogi Collaboration

Sage Therapeutics™

Brain Health Disorders — Global Healthcare Challenge

In 10 years, Sage has expanded the potential for solutions and through collaborations expects to further accelerate and expand estimated patient reach

18M
Sage

22M
Sage + Shionogi

>450M
Sage + Shionogi + Biogen
+ potential acceleration of Sage proprietary programs

- Huntington's Disease
- Alzheimer's Disease and other Dementias
- Epilepsy
- Treatment Resistant Depression
- Bipolar Depression
- General Anxiety Disorder
- Parkinson's Disease
- Essential Tremor

- Postpartum Depression
- Major Depressive Disorder

Shionogi Collaboration

2020 Biogen Collaboration

Sage Therapeutics™

Patients Have Been Told Too Long
"*This is as good as it gets -- deal with it*"

Loss of: vitality, quality of life, independence, reaching full potential, life expectancy

Family function *Caregiver burnout* *Workplace challenges*

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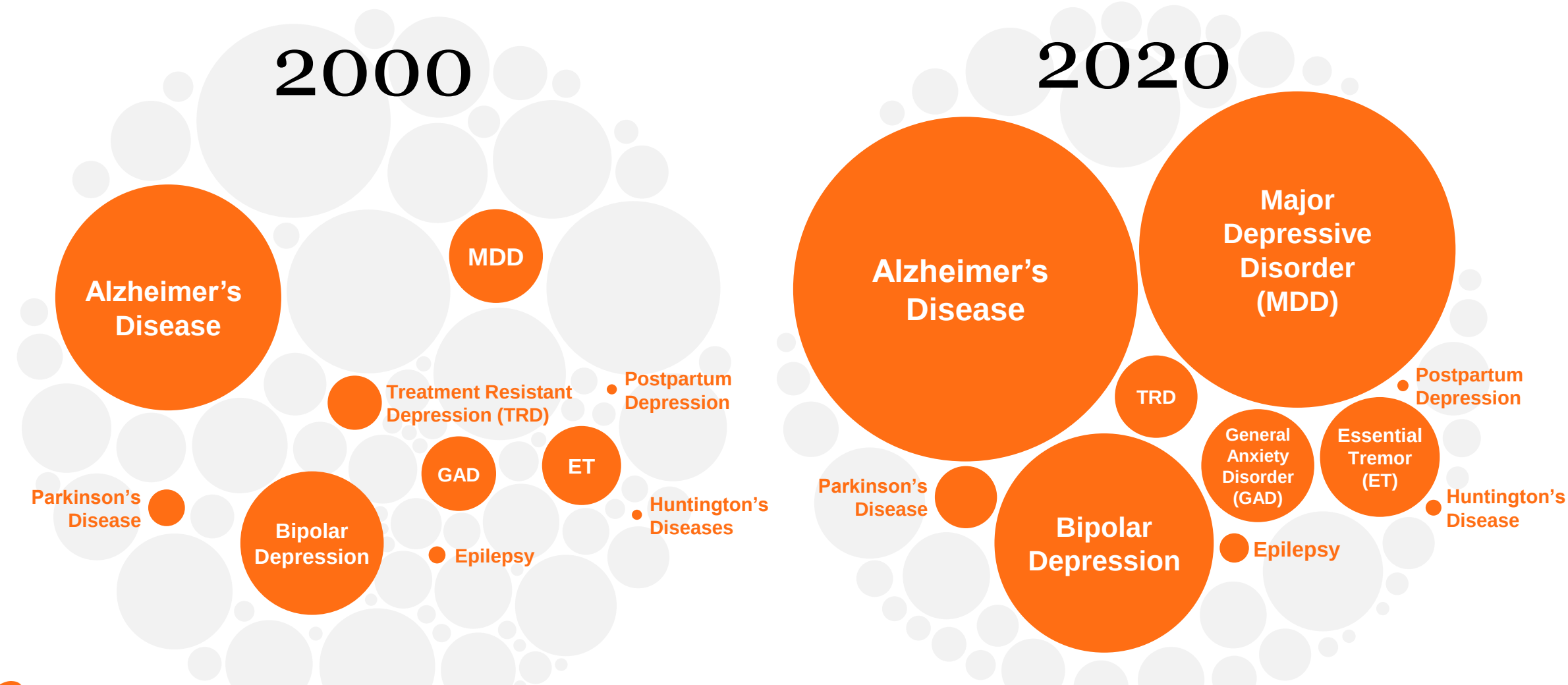
Economic and Societal Impact of Brain Health Disorders in the U.S.

Urgent Need for Innovation



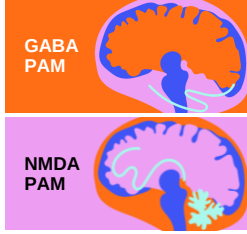
BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2020 economic burden amounts using U.S. specific studies in respect to the indications noted.

Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, TRD = treatment resistant depression, GAD = generalized anxiety disorder, BPD = bipolar depression, ET = essential tremor, HD = Huntington's disease, PD = Parkinson's disease

Sage's innovative product engine is designed to create a consistent and sustainable flow of products with the potential for **big effects** on brain health disorders for millions of patients

Imagine a world where the status quo isn't good enough…

Expanding and accelerating our Brain Health franchises with goal of addressing critical unmet patient need

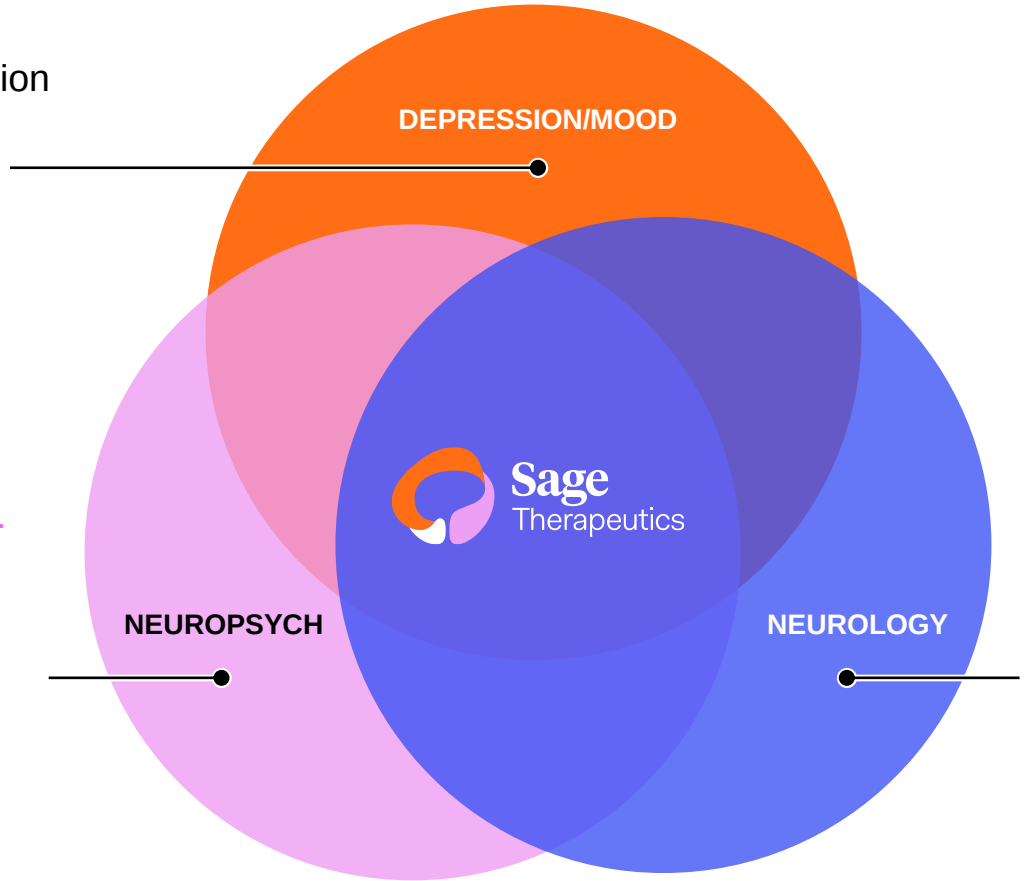


ZULRESSO | SAGE-217*

- First and only company with approved postpartum depression option
- Establish anchor program in major depressive disorder with potential to change treatment paradigm
- Novel mechanism and first-in-class GABA positive allosteric modulators with varying routes of administration

SAGE-718 | SAGE-904 | SAGE-421

- First-in-class Oxysterol-based NMDAr modulators
- Strong preclinical basis for role of NMDA receptor system in cognition
- Multiple diseases associated with low NMDA function



SAGE-324* | **SAGE-689 | SAGE-319**

- Promising signals of tremor reduction
- Targeting rare epilepsy disorders as potential parallel program
- Potent anti-seizure, anxiolytic and anticonvulsant preclinical data

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*Collaboration products

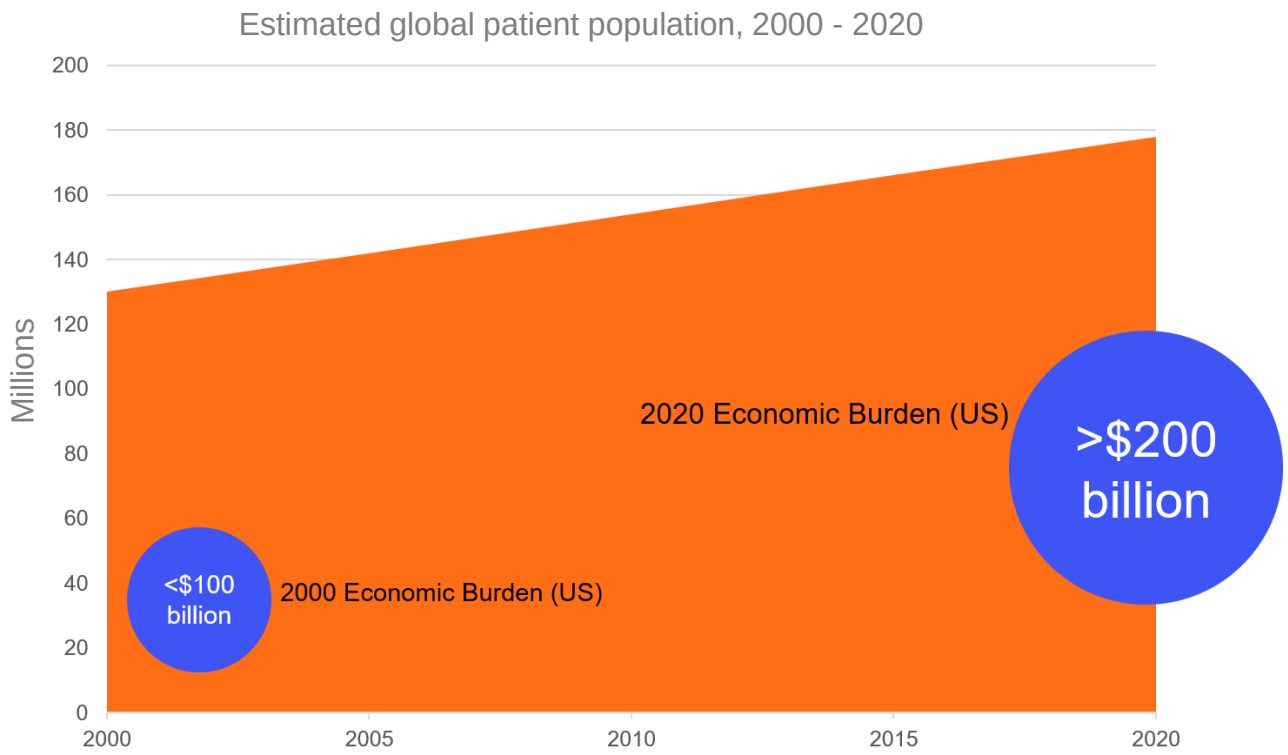
A Leading Brain Health Portfolio

Light shades indicate trials in the planning or evaluation stage

Depression and Mood Disorders

Paucity of innovation plagues disease landscape with significant unmet need

- Despite new classes of medicines developed to treat depression in last 60 years, **prevalence and impact continue to increase globally**
  - > 50% of patients suffer **severe impact on ability to function**
  - Depression shown to **have generational impact** as well as direct impact on caregivers (e.g., caregivers/ partners unable to work full time, increasing economic burden exponentially)
  - Rates continue to increase, particularly in young adults
- Increasing evidence that depression and some **mood disorders are episodic events** caused by many triggers (e.g., genetics, postpartum, COVID)
- Sage believes patients can be **treated episodically and/or as needed, reducing burden of chronic management**



BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2020 economic burden using U.S. specific studies in respect to the indications noted.

Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, TRD = treatment resistant depression, GAD = generalized anxiety disorder, BPD = bipolar depression

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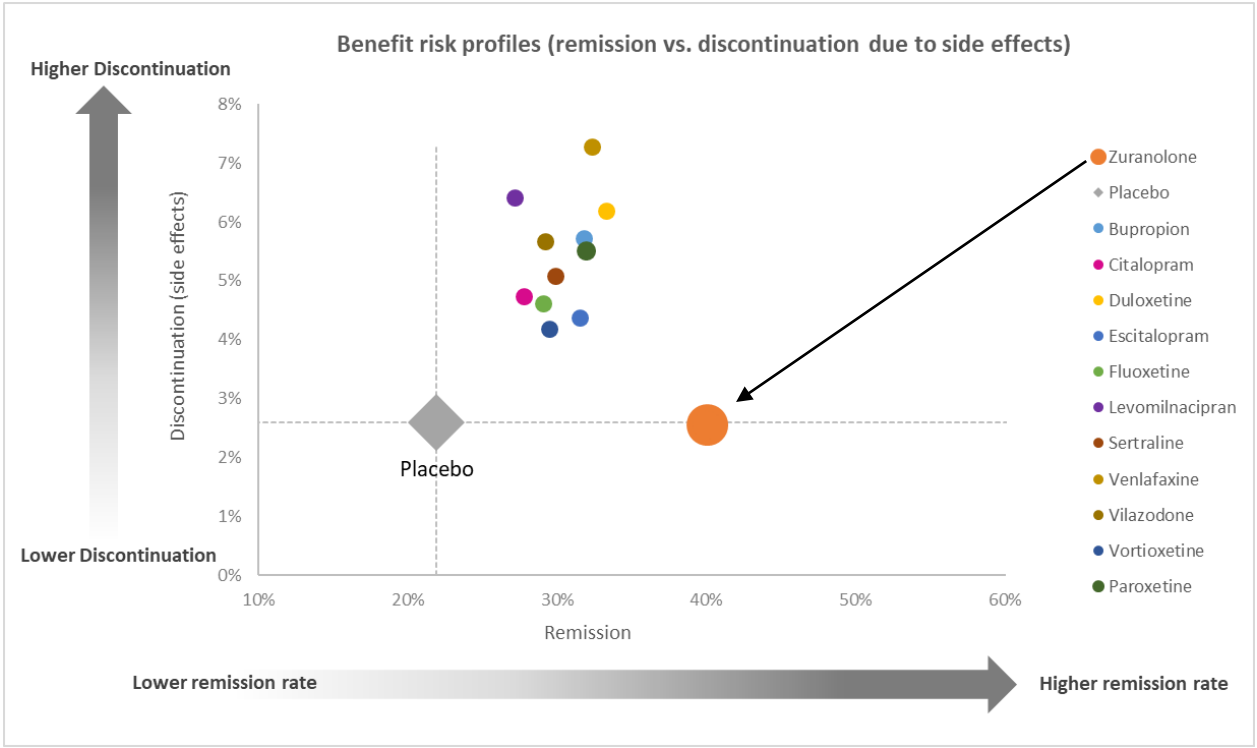
Paucity of innovation plagues patient journey to find effective treatment for depression and mood disorders

- Benefit/risk profile of treatments for major depressive disorder remains unchanged despite at least 35 approved treatments in last 30 years
- Increasing burden and unmet need supports development of more innovative treatments
- In clinical trials to date:
  - Zuranolone demonstrated a reduction of depressive symptoms seen within 72 hours
  - 70% of subjects treated with zuranolone in the SHORELINE study interim data cut (30 mg) **required 2 or fewer treatments** in a year
  - **Zuranolone has been generally well-tolerated** in more than 3,000 subjects to date

Benefit (remission) vs. Risk (discontinuation)
(integrated set 201B & MOUNTAIN ≥24 compared to SoC)



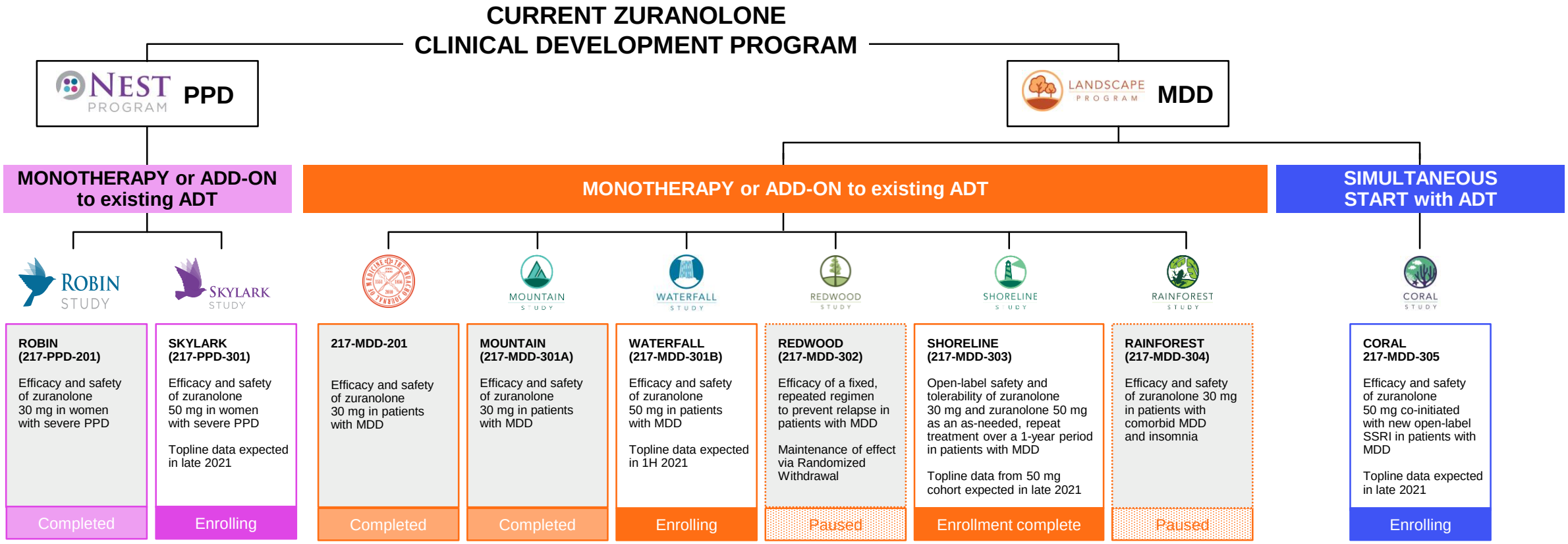
Comparison to SOC was carried out through a Bucher ITC using Cipriani 2018[1]. There are assumptions and limitations associated with this analysis.

Variations in study design across the included trials may limit the generalizability of results.

[1]Cipriani, 2018 Lancet

Zuranolone's Landscape Program

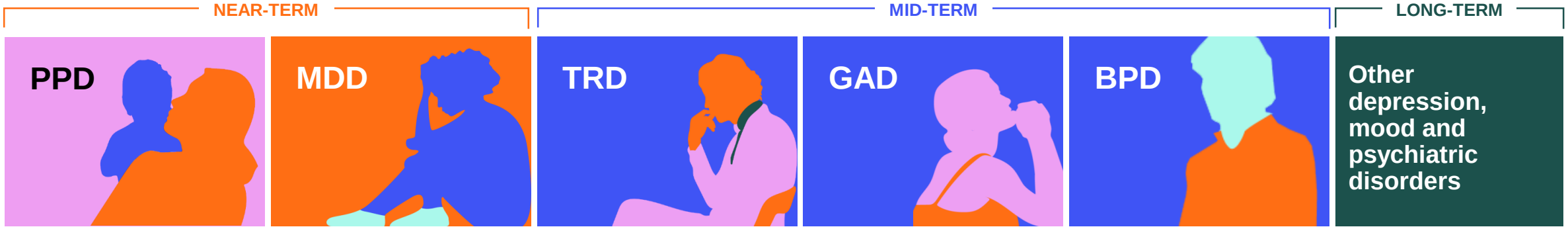
Potential to reshape the depression landscape



Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, ADT = antidepressant therapy

Zuranolone is a Sage-created innovation with potential to impact millions globally

Development plan has potential to be accelerated by strategic collaboration with Biogen



	2021 Early	2021 Mid	2021 Late	*Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4
DEPRESSION FRANCHISE				**Expected milestones:**
Zuranolone (Sage-217)		●		Report topline data from WATERFALL Study in major depressive disorder **(1H21)**
		●		Report full data from SHORELINE Study 30 mg cohort in major depressive disorder
			●	Report topline data from SKYLARK Study in postpartum depression
			●	Report topline data from CORAL Study in major depressive disorder for rapid response treatment when co-initiated with new antidepressant therapy
			●	Report topline data from SHORELINE Study 50 mg cohort in major depressive disorder

Composition of Matter Patent through 2034, subject to potential extensions

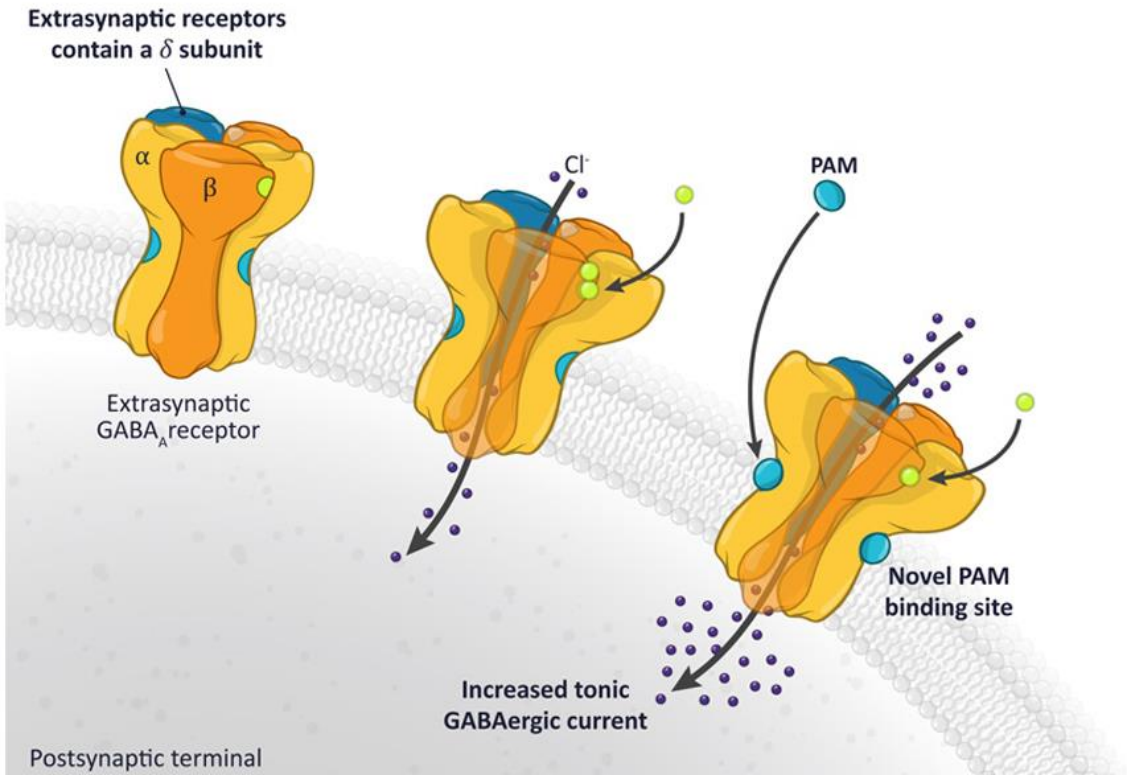
Sage Therapeutics™ Biogen SHIONOGI

Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, TRD = treatment resistant depression, GAD = generalized anxiety disorder, BPD = bipolar depression

Sage taking on need for innovation beyond mood disorders

Novel product candidates being evaluated for neurological conditions

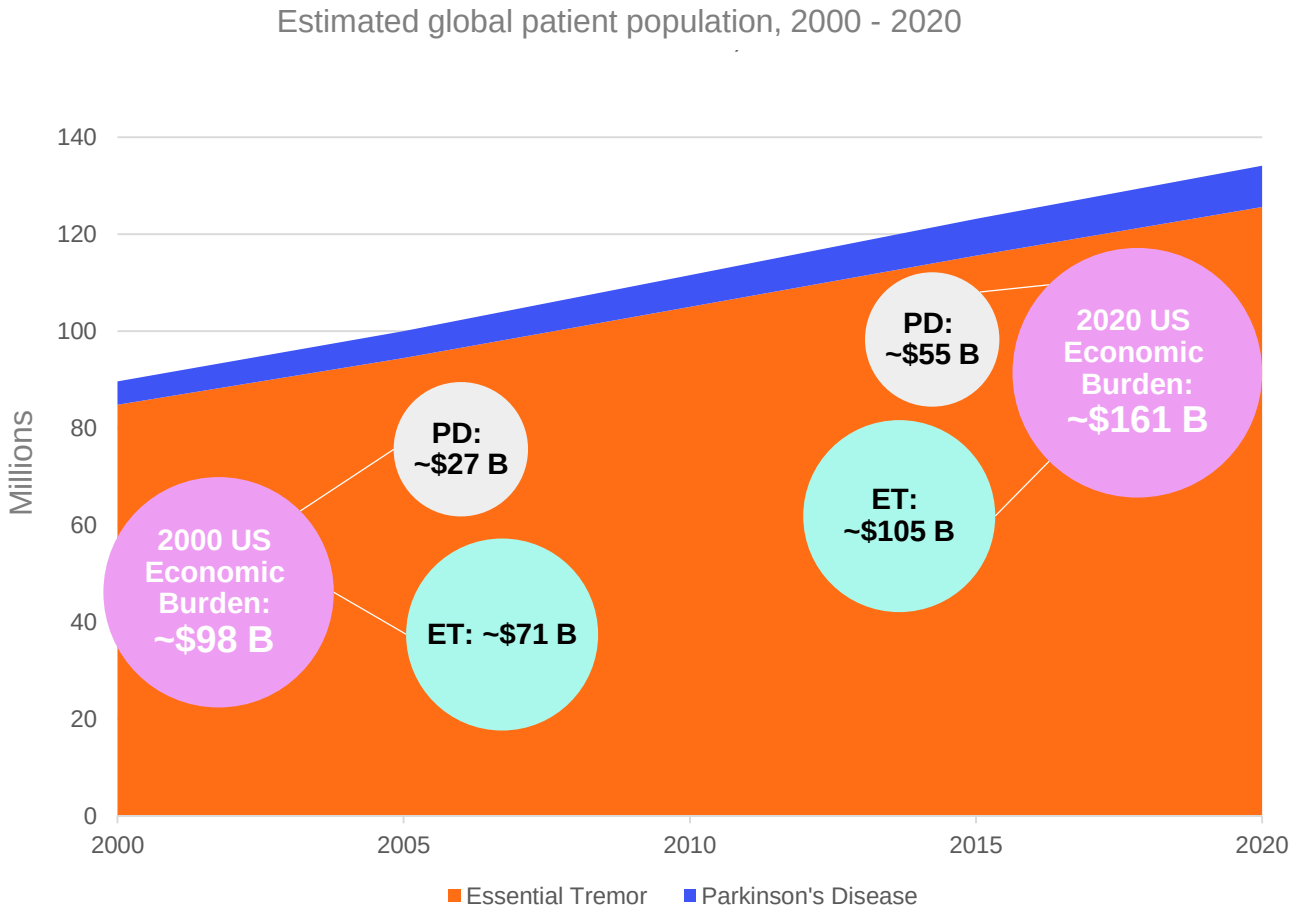
- Novel positive allosteric modulators (PAM) of $GABA_A$ receptors with potential to support development in multiple indications
- Predictable pharmacodynamic effects with ability to tune formulation and potency — currently via oral, IV, or IM dosing
- High selectivity with decreased off-target effect
- Sage $GABA_A$ PAMs include SAGE-324, a potential therapy for neurological conditions such as essential tremor, epilepsy, and Parkinson's disease



Movement and neurological disorders

Gaps remain in bringing effective treatments to people with movement disorders

- Standards of care are inadequate for many people suffering from debilitating movement disorders
  - It's estimated that nearly 135 million people globally suffer from essential tremor (ET) or Parkinson's disease (PD)
- Movement disorders can make the simplest activities of daily life difficult, if not impossible
  - Chewing, eating, standing, walking, self-care
- Substantial mental health impact and caregiver burden
  - Depression/low mood, anxiety, poor sleep
- Sage has demonstrated that the GABA positive allosteric modulation mechanism is important in movement disorders



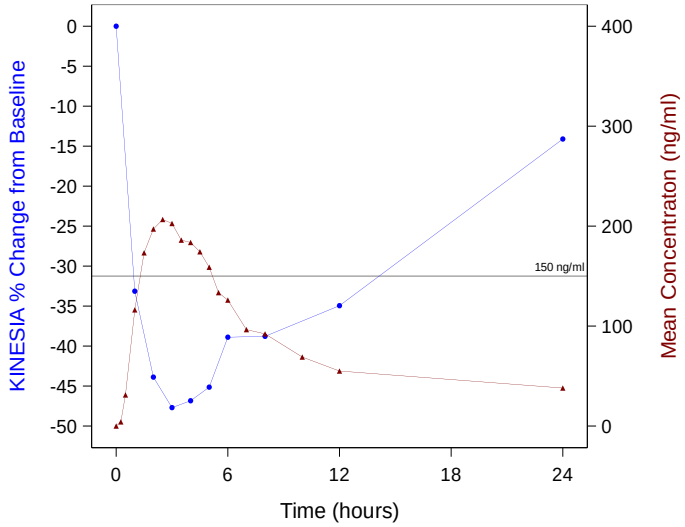
BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2020 economic burden using U.S. specific studies in respect to the indications noted.

SAGE-324: Novel potential treatment for movement disorders

Predictable PD effects and PK profile with long half-life

- SAGE-324 is well-suited for development in essential tremor (ET):
  - Most prevalent movement disorder in the US (est. 6M+)
  - Last pharmacological treatment for ET was approved in 1967
  - High unmet need; 50% of treated patients do not respond or have sub-optimal response to standard of care
- In an open-label, phase 1 study, a single dose of SAGE-324 resulted in nearly 50% tremor reduction in ET patients, demonstrated on measure most closely associated with disability
- Good oral bioavailability and long half-life provides flexibility in dosing paradigms for potential development in additional disorders including Parkinson's disease and epilepsies

Total upper limb combined score after single dose in 6 people with ET as measured by accelerometer



PK over time in 6 people with ET dosed with SAGE-324

- Clear PK/PD relationship
- Promising signals of tremor reduction, consistent with those observed previously for brexanolone and SAGE-217
- Well-tolerated in Phase 1 study: most common AEs (≥5%) included somnolence, dizziness, and feeling of relaxation

Sage Therapeutics™ Biogen

GABA PAM

Sage-created innovation with potential to impact millions globally

Development plan has potential to be accelerated by strategic collaboration with Biogen

MID-TERM

LONG-TERM

Essential Tremor

Parkinson's Disease

Epilepsies

Other movement and neurological disorders

2021

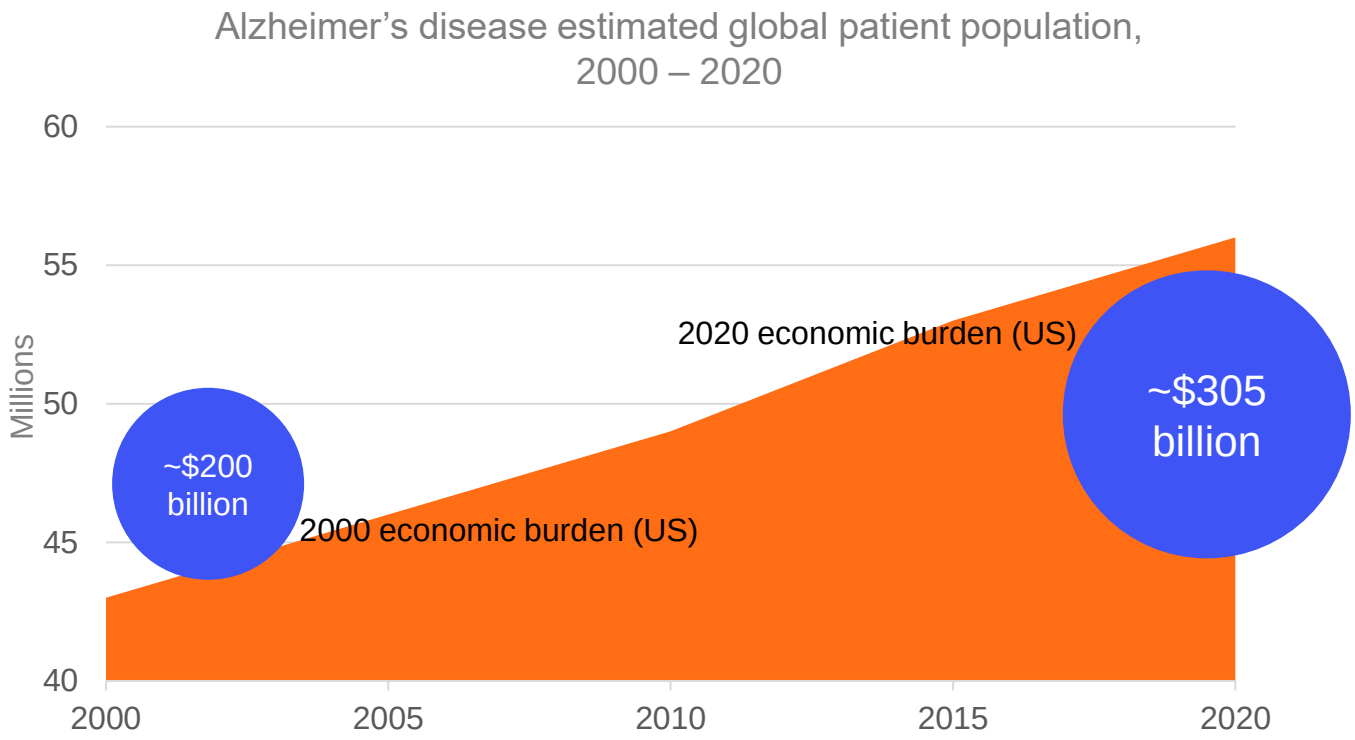
	Early	Mid	Late	*Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4
NEUROLOGY FRANCHISE				**Expected milestones:**
SAGE-324	●			Report topline data from KINETIC Study in essential tremor
			●	Initiate Phase 2b study in essential tremor

Sage Therapeutics™ Biogen

Neuropsychiatric Disorders

Dearth of innovative treatments approved for disorders of cognition

- Globally, disorders involving cognitive dysfunction continue to increase and are one of the greatest areas of unmet need
  - Currently available treatments are limited in efficacy
- People with cognitive impairment report:
  - Executive deficits: multi-tasking, organization, planning, working memory
  - Difficulty concentrating
  - Memory loss
- Significant impact on patient ability to work, live independently, adhere to medical care, and interact with family



Sage Therapeutics™

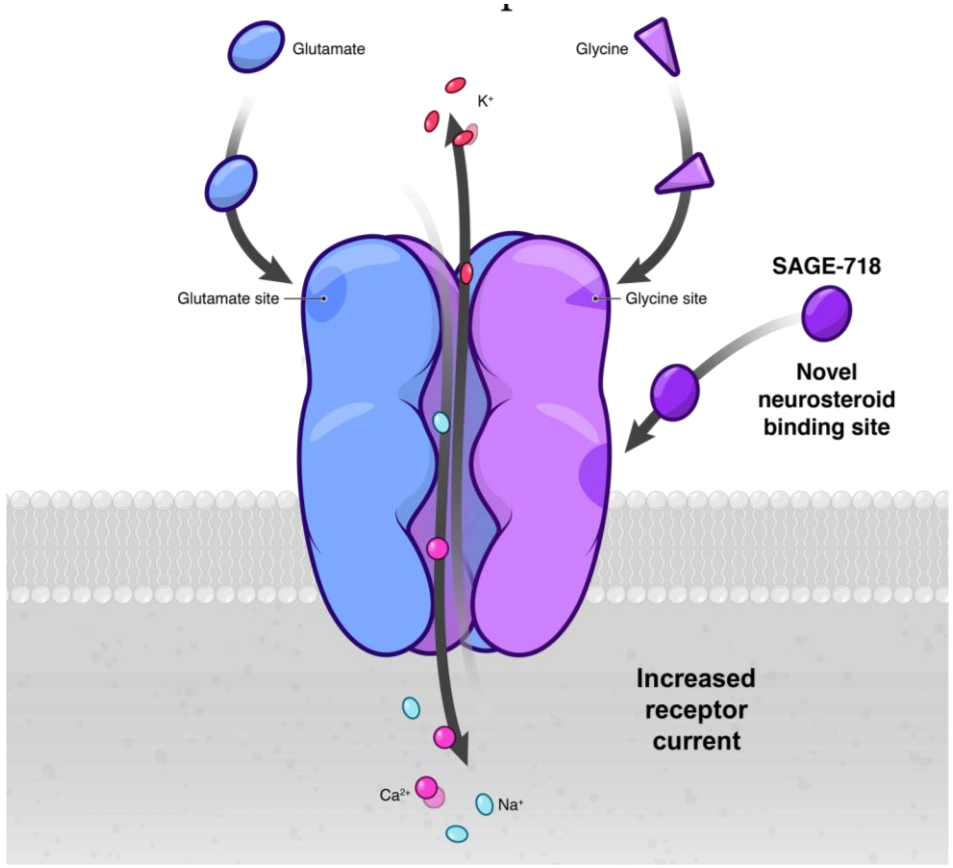
BLS CPI (Consumer Price Index) Calculator was used to estimate 2000 and 2020 economic burden using U.S. specific studies in respect to the indications noted.

Re-thinking Treatment of Neuropsychiatric Disorders

Sage has developed a robust library of NMDA receptor modulators

- NMDA receptors play a critical role in the process of neuroplasticity and are important in a host of cognitive, learning and behavioral processes
  - NMDA receptor function can be reduced by disease and declines during aging
- NMDA positive allosteric modulators (PAMs) may have potential to address disorders of cognition & behavior across the lifespan:
  - Neurodegenerative disorders
  - Neurodevelopmental disorders
  - Disorders requiring recovery or rehabilitation of cognitive function
- Sage has developed a library of novel, wholly-owned, NMDA modulators with unique profiles, including SAGE-718
- Biomarkers identified by Sage may inform development

Endogenous & Exogenous Ligands at the NMDA Receptor



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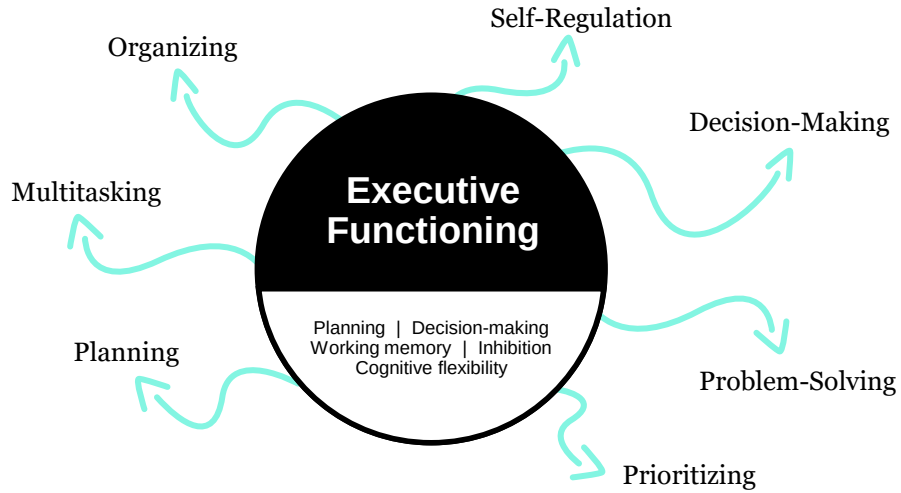
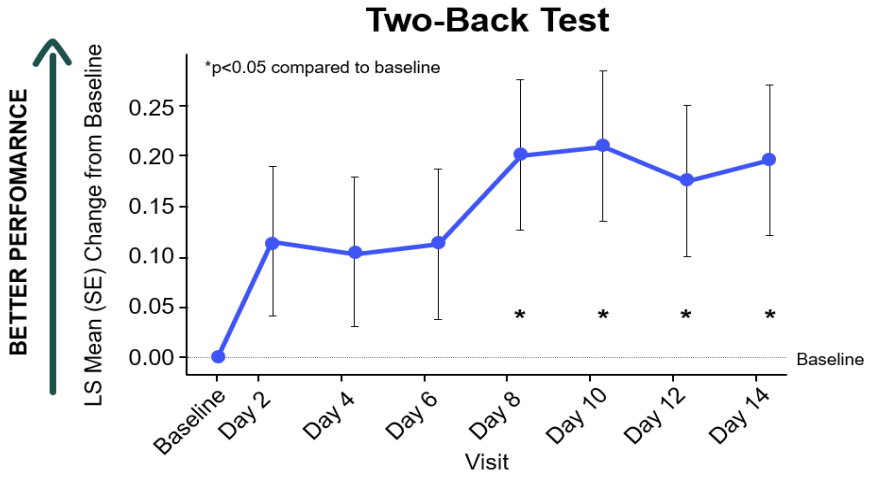
SAGE-718: Improving cognitive and executive function

Potential to provide unique cognitive benefits for patients with neurodegenerative disorders

- SAGE-718 profile well-suited for study of potential to benefit executive function in patients with neurodegenerative disorders:
  - Clinical findings from Phase 1 studies suggest potential to improve executive function, a key component of brain health across life-span
- Ongoing exploration in areas of cognitive dysfunction in diseases with high unmet need, including Alzheimer's, Parkinson's, and Huntington's disease
- Five phase 1 studies to date – generally well-tolerated and with meaningful activity suggesting potential in brain health disorders





Cognitive Performance in Patients w/ Early Huntington's Disease Treated with Open-Label SAGE-718

Sage Therapeutics™

Sage-created innovation with potential to impact millions globally

Collaboration provides resources for acceleration of plans for internal pipeline, including SAGE-718

MID-TERM

LONG-TERM

Parkinson's Disease Cognitive Dysfunction

Alzheimer's Disease Cognitive Dysfunction

Huntington's Disease Cognitive Dysfunction

Other conditions with impaired cognitive/executive dysfunction

2021

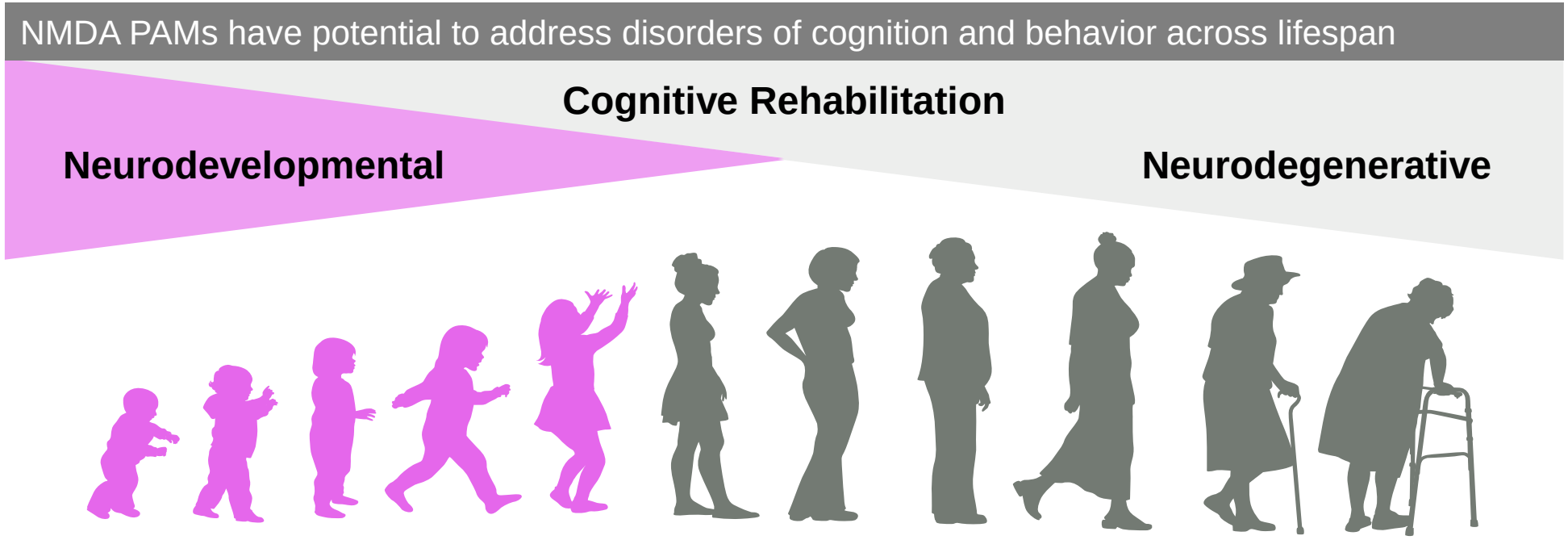
	Early	Mid	Late	*Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4
NEUROSPYCHIATRY FRANCHISE				**Expected milestones:**
SAGE-718	●			Report topline data from PARADIGM Study in Parkinson's disease cognitive dysfunction
	●			Initiate LUMINARY Study in Alzheimer's disease cognitive dysfunction
			●	Report topline data from LUMINARY Study in Alzheimer's disease cognitive dysfunction
			●	Initiate placebo-controlled Phase 2 study

Sage Therapeutics™

Sage proprietary product engine

SAGE-904: Differentiated NMDA PAM profile

Pharmacological profile suited for study in neurodevelopmental therapeutics



- SAGE-904 designed for potential use as ***neurodevelopmental*** therapy
- Druglike profile supporting once-daily, oral, chronic dosing
- Phase 1 studies to inform selection of development path

SAGE-689: Rapid acting, intramuscular GABA PAM

Multiple opportunities in diseases with high unmet need

- Potent preclinical anxiolytic and anticonvulsant activity
- Rapid absorption and good bioavailability following *intramuscular* administration
- Phase 1 translational studies designed to accelerate specific indication selection
- Formulation flexibility and high intrinsic solubility enables multiple potential pathways based on patient needs
  - Acute use with faster onset may provide opportunities in areas like agitation or social anxiety

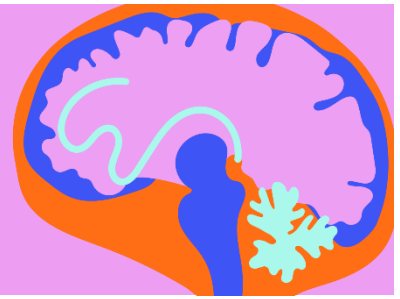
Continuing Innovation with the GABA and NMDA platforms

Preclinical profile of SAGE-319
GABA PAM

- Potent, extra-synaptic $GABA_A$ receptor preferring positive allosteric modulator
- Druglike profile supporting daily, oral, chronic dosing
- Differentiated EEG signature compared to SAGE-217 and SAGE-324

Potential indications:
DISORDERS OF SOCIAL INTERACTION

Preclinical profile of SAGE-421
NMDA PAM



- Potent NMDA receptor positive allosteric modulator
- Druglike profile supporting daily, oral, chronic dosing

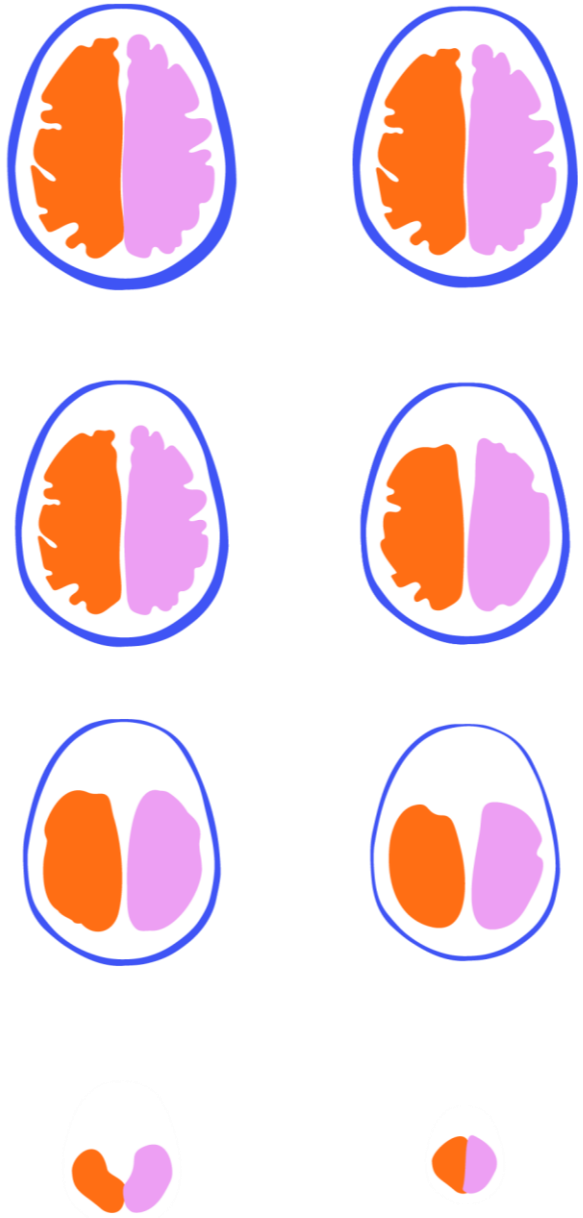
Potential indications:
NEURODEVELOPMENTAL DISORDER

Sage Therapeutics™

Proactive, predictive and productive drug development approach:

Enables product engine and portfolio expansion into diseases with high unmet needs

- Sage is a leader in NAS and oxysterol chemistry with >8K compound library and >50 patent applications
- Focus on understanding how to modify circuitry that impacts brain function at the network level
- Robust engine for turning early ideas into clinical proof-of-concept rapidly



Sage Therapeutics™

Anticipated 2021 Milestones

*Early:Q1-Q2; Mid:Q2-Q3; Late: Q3-Q4

	Early	Mid	Late	
DEPRESSION FRANCHISE				
Zuranolone (Sage-217)		●		Report topline data from WATERFALL Study in major depressive disorder (1H21)
		●		Report full data from SHORELINE Study 30 mg cohort in major depressive disorder
			●	Report topline data from SKYLARK Study in postpartum depression
			●	Report topline data from CORAL Study for rapid response treatment
			●	Report topline data from SHORELINE Study 50 mg cohort in major depressive disorder
NEUROLOGY FRANCHISE				
SAGE-324	●			Report topline data from KINETIC Study in essential tremor
			●	Initiate Phase 2b study in essential tremor
NEUROSPYCHIATRY FRANCHISE				
SAGE-718	●			Report topline data from PARADIGM Study in Parkinson's disease cognitive dysfunction
	●			Initiate LUMINARY Study in Alzheimer's disease cognitive dysfunction
			●	Report topline data from LUMINARY Study in Alzheimer's disease cognitive dysfunction
			●	Initiate placebo-controlled Phase 2 study
EARLY DEVELOPMENT				
SAGE-689			●	Complete Phase 1 SAD study
SAGE-904			●	Complete Phase 1 studies
OTHER DEVELOPMENT OPPORTUNITIES				
Brexanolone			●	Report topline data from study in COVID-19 related acute respiratory distress syndrome
Product Engine		**By 2023**		Capable of delivering 2+ IND-enabling compounds per year

Sage is a leader in brain health – *making medicines that matter*

Disciplined execution in 2020 created strong foundation for near, mid, and long-term value-creation potential for patients and shareholders

Leading brain health pipeline spanning three core franchises, each with differentiated assets with goal of delivering two or more IND-enabling compounds per year, starting in 2023

Catalyst rich 2021 includes meaningful data flow across all franchises

Expertise in place to focus on successful patient access and global commercial execution if product candidates are approved

Financial flexibility enables continued investment in innovation, with mission of creating top-tier biopharma in 5 years

Sage Therapeutics™

Seeing the brain differently *makes a world of difference*

Sage Therapeutics™