Our Goal Through Strategic Collaboration with SAGE

February 5, 2019

SAGE Therapeutics Inc.

Shionogi & Co., Ltd.

SHIONOGI

Agenda

1. **Our Goal Through Strategic Collaboration with SAGE**
   - **Isao Teshirogi**, Ph.D., President and CEO, Shionogi
2. **Strategic Collaboration with Shionogi**
   - **Jeffrey Jonas, M.D.,** Chief Executive Officer, SAGE Therapeutics Inc.
3. **Strength of Shionogi's Research in CNS Area**
   - **Takeshi Shiota**, Ph.D., Senior Vice President Pharmaceutical Research Division, Shionogi
4. **Development of S-812217 in Japan**
   - **Jun Yoshimoto**, D.V.M., Ph.D. Vice President, Project Management Department, Global Development Division, Shionogi
5. **Q&A**

Our Goal Through Strategic Collaboration with SAGE

Isao Teshirogi, Ph.D.
President and CEO

SHIONOGI

Growth Strategy for 2020

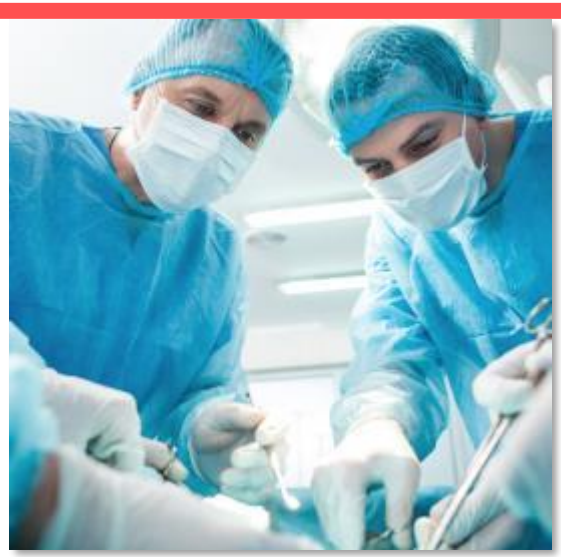
Grow sustainably as a drug discovery-based pharmaceutical company contributing to a more vigorous society through improved healthcare

Region/Area to grow	Keys to grow
Japan/US Development in EU/Asia	**Addressing society's needs**
Infectious disease **Pain/CNS**	**Balance of innovation and health economic efficiency**

Social Challenges that Shionogi Strives to Address

Creating a more vigorous society

- Help people who are isolated due to pain/suffering to re-enter society
- Provide relief from psychological uncertainty allowing fulfillment of one's innate ability
- Maintain the dignity of the individual through all the stages of life



- Develop new drugs against infectious diseases that lack effective medical treatments
- Reduce outbreaks of bacterial and viral resistance by promoting proper use of anti-infective drugs

Protecting people from the threat of infectious diseases

Produce Next-Generation Drugs in CNS Area Through Collaboration with Business Partners

SONG for you!

Preclinical | Phase I | Phase II, III

CNS

Collaboration

S-812217

Depression

- Breakthrough profiles
- FDA designated Break-Through Therapy in US

SAGE THERAPEUTICS

Steady progress of development for "postpartum depression" and "major depression disorder" in the U.S.

Plan to initiate clinical study in patients in FY2019 in Japan

BPN14770

Drug candidate for cognitive and memory deficits

Fragile X Syndrome、Alzheimer's disease

SK PJ

Alzheimer's disease, mental disorder

Peptide project

PDC

(Peptide Drug Conjugate)

Platform for delivery of chemical compounds to the brain

SAGE THERAPEUTICS

SHIONOGI

Good Collaboration for Brighter Future

SAGE THERAPEUTICS

5 February 2019

Strategic Collaboration with Shionogi

Rethinking CNS

Safe Harbor Statement

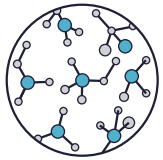
The slides presented today and the accompanying oral presentations contain forward-looking statements, which may be identified by the use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “opportunity”, “potential,” or “continue,” and other similar expressions. Forward-looking statements in this presentation include statements regarding: our expectations regarding the potential for approval by the FDA of our NDA submission for ZULRESSO; our expectations as to the timing of a potential approval and launch; our planned commercial activities, goals and strategy, if ZULRESSO is approved; our anticipated development activities and timelines; the estimated number of patients with certain disorders or diseases or that may benefit from our drugs in the future; the potential for development of our other products candidates in various indications; the target product profile and goals for our product candidates and their potential to change treatment paradigms and improve lives, if we are successful; and our views on our ability to become the leading CNS 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:

- The FDA may not approve ZULRESSO and may require additional trials, analyses or data;
- Even if ZULRESSO is approved, we may encounter issues, delays or unexpected challenges in launching or commercializing the product, including issues related to timing of DEA scheduling, issues related to market acceptance and reimbursement, challenges associated with restrictions or conditions that may be imposed by regulatory authorities, including challenges related to limiting the site of administration to a certified healthcare facility monitored by a qualified healthcare provider, and the necessity for a REMS; and challenges associated with the execution of our sales and patient support activities, which in each case could limit the potential of our product;
- Success in pre-clinical studies or in early stage clinical trials may not be repeated or observed in ongoing or future studies involving the same compound or other product candidates, and future pre-clinical and clinical results for our product candidates 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;
- Even if our planned development programs are successful, we still may not achieve review or approval;
- 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;
- 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;
- We may encounter unexpected safety or tolerability issues with respect to any of our product candidates;
- 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 products are being developed;
- Our operating expenses may be higher than forecasted, and we may also face unexpected expenditures or decide to expand our activities, in either case which may result in the need for additional funding to support our business activities earlier than anticipated;
- Funding to support operations may not be available, when needed, on reasonable terms or at all, or may result in significant dilution to existing shareholders;
- 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.

For additional disclosure regarding these and other risks Sage faces, see the disclosure contained in the "Risk Factors" section of our most recent quarterly 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.

This presentation does not constitute an offer, recommendation, general solicitation or official confirmation of terms. We do not guarantee the information in this presentation is accurate or complete. This presentation does not constitute advice or an expression as to whether a particular security or financial instrument is appropriate for you and meets your financial objectives; such matters should be discussed with your advisors and/or counsel.

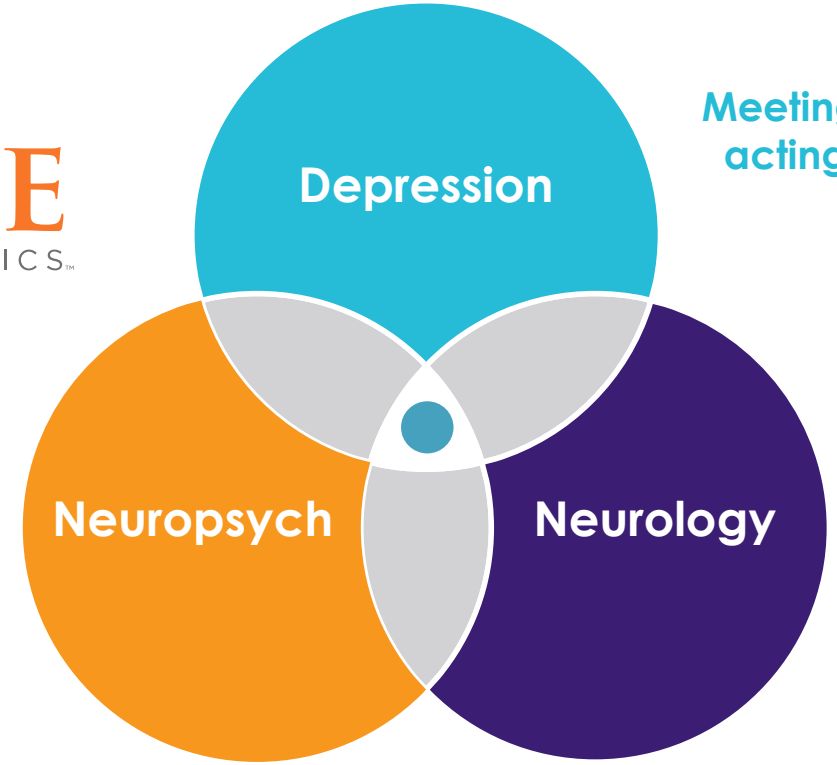
Successfully Establishing a Leading CNS Company in 8 Years

	 CLINICAL PRODUCT CANDIDATES	 CLINICAL INDICATIONS	 LIBRARY COMPOUNDS	 FINANCING
2011	0	0	0	$35M Series A
2014	1	1	>1k	$117M IPO
2019	4	7	>6K	~$6.7B Market cap[1]

1. As of market close on 31 Jan. 2019

Establishing a Multi-Franchise CNS Company

SAGE THERAPEUTICS



Meeting unmet need for rapid-acting treatment-as-needed

Exploring 1st-in-class approach for cognition-related disorders

Exploring novel mechanism for chronic diseases

Building a Unique Depression Franchise

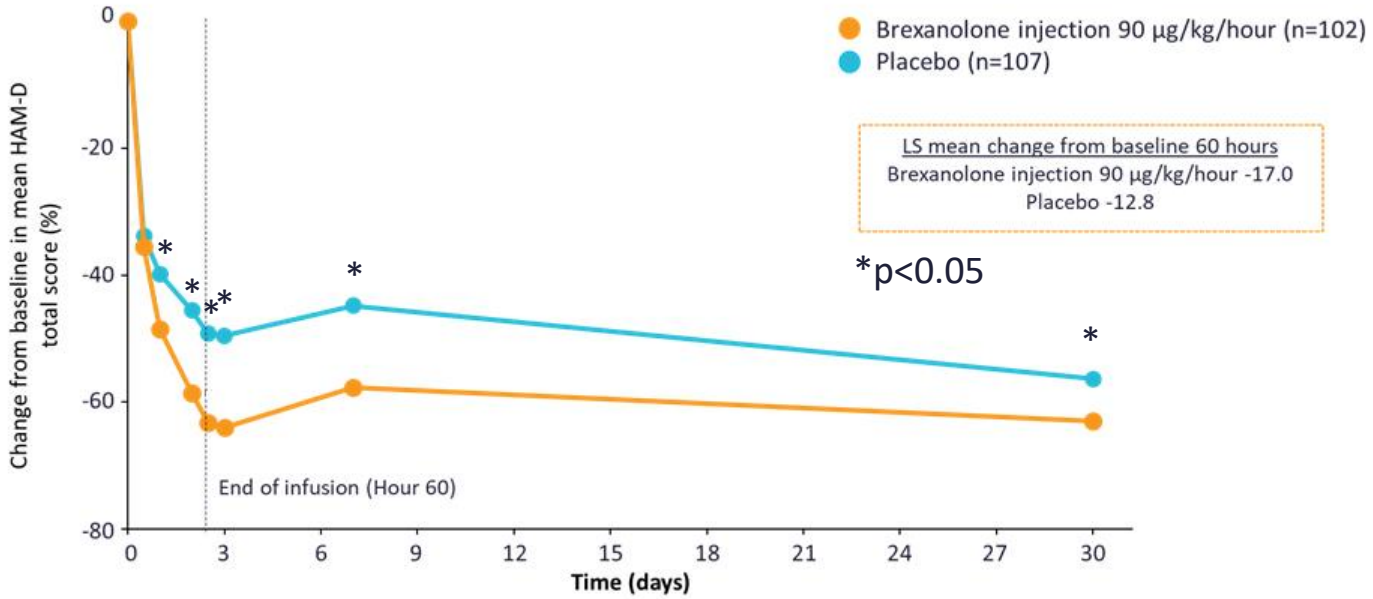
1st-in-class approach to treat mood disorders with the goal of rapid-acting short course therapy

Potential for ZULRESSO™ (brexanolone) injection to be first therapy specifically indicated for PPD

Broad opportunity with SAGE-217 to impact millions of patients

ZULRESSO™ (brexanolone) Injection in PPD

Integrated Hummingbird Study Data Demonstrate Rapid and Durable HAM-D Reduction



ZULRESSO was generally well tolerated in all three studies. The most common AEs were headache, somnolence/sedation and dizziness/vertigo. The most common adverse events leading to dose reduction or interruption were related to sedation (including loss of consciousness) or the infusion site.

HUMMINGBIRD STUDY

ZULRESSO Approval Would Provide Opportunity to Take on Stigma of PPD

- PPD is the most common medical complication of childbirth
- ZULRESSO is the first medicine under FDA review specifically for the treatment of PPD
- PPD can lead to devastating consequences for a woman and for her family
- Suicide is the leading cause of maternal death following childbirth

>400K **Women experience PPD** each year in the US

~50% **of patients are currently diagnosed and treated**

25-30% **are severe**

1. CDC, https://www.cdc.gov/mmwr/volumes/66/wr/mm6606a1.htm, 2017. 2. Bonthapally, ISPOR Annual International meeting, 2017. 3. PACT, The Lancet, 2015. 4. McCabe-Beane, Journal of Reproductive and Infant Psychology, 2016. All estimates represent management's assessment of total number of patients in U.S. based on relevant literature. Other estimates exist in the literature or using claims analysis which are smaller than our estimates. We attribute differences to differences in methodologies and other factors. As a result, more in-depth studies are needed to better understand prevalence in each case.

Strategic SAGE-217 Collaboration with Shionogi

Potential to Accelerate Development and Commercialization of SAGE-217 in Key Asian Markets

SAGE THERAPEUTICS

Expansion of Sage's Global Footprint

- Goal of collaboration to accelerate development of a potentially groundbreaking medicine to patients in key Asian markets
- Sage maintains exclusive rights to develop and commercialize SAGE-217 outside of those geographies

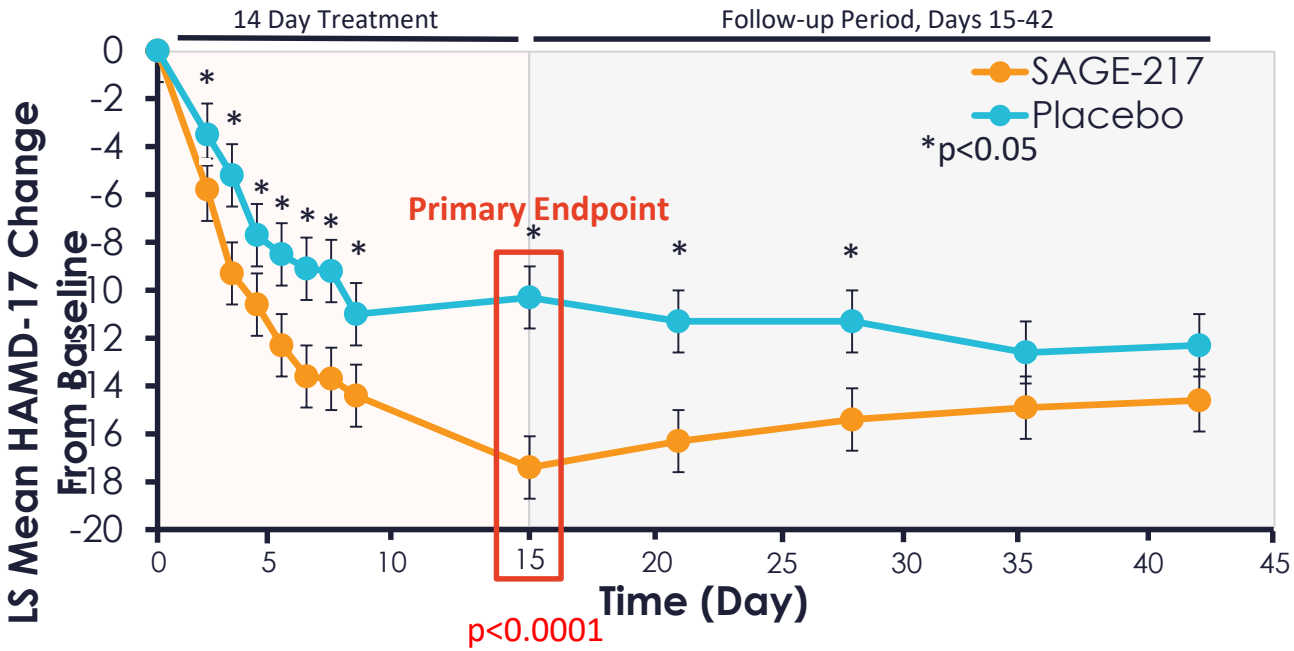
SHIONOGI

Expert Partner in Key Asian Markets

- Shionogi is responsible for clinical development and commercialization of SAGE-217 in Japan, Taiwan, and South Korea
- Shionogi has strong presence in Asia in developing & commercializing therapeutics for CNS disorders

SAGE-217: Positive Pivotal **MDD** Results (MDD-201)

Demonstrated Rapid, Profound and Durable Treatment Response

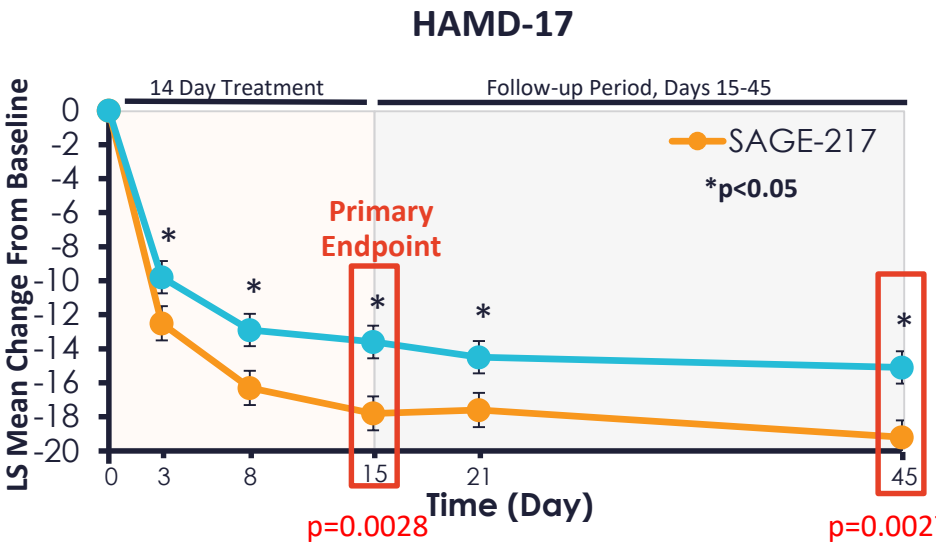


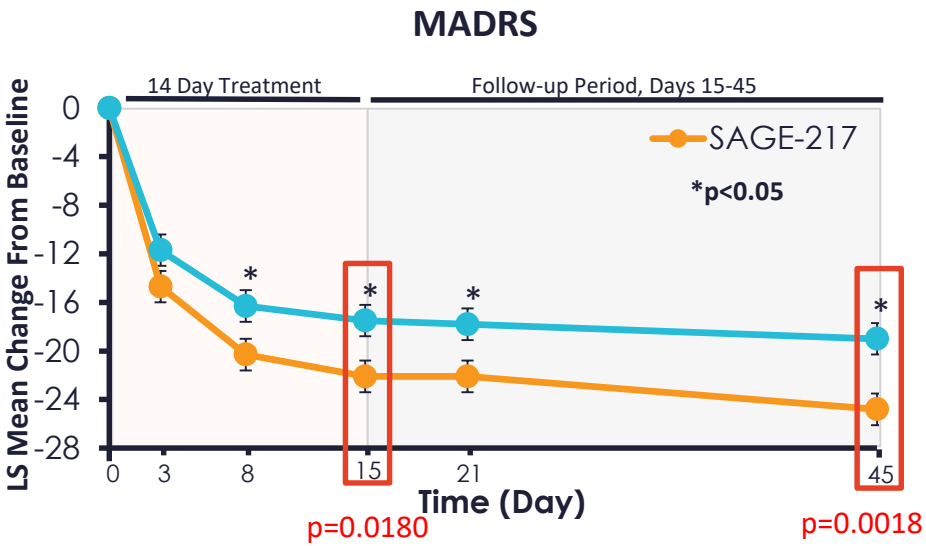
SAGE-217 was generally well-tolerated in the study. The most common AEs included headache, dizziness, nausea and somnolence.

SAGE-217: Positive Phase 3 **PPD** Results (PPD-201)

Statistically Significant HAMD-17 Improvement Observed on Day 3 and Maintained through Day 45; Improvement in MADRS Scale Consistent with HAMD-17 Results

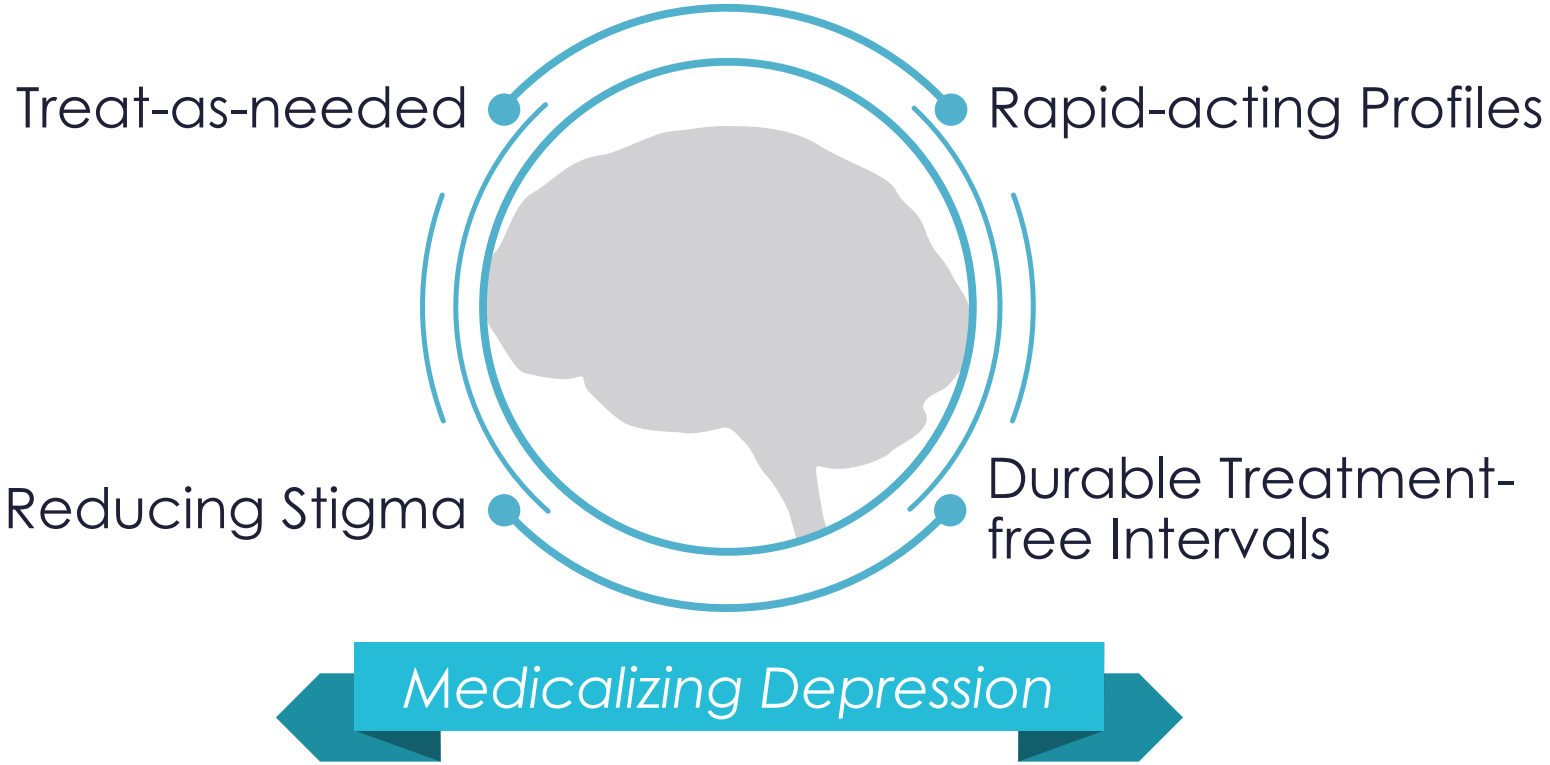
ROBIN STUDY





SAGE-217 was generally well-tolerated in the study. The most common adverse events (>5%) in the SAGE-217 treatment group were somnolence, headache, dizziness, upper respiratory tract infection, diarrhea, and sedation. Two subjects experienced SAEs, one subject in each treatment group.

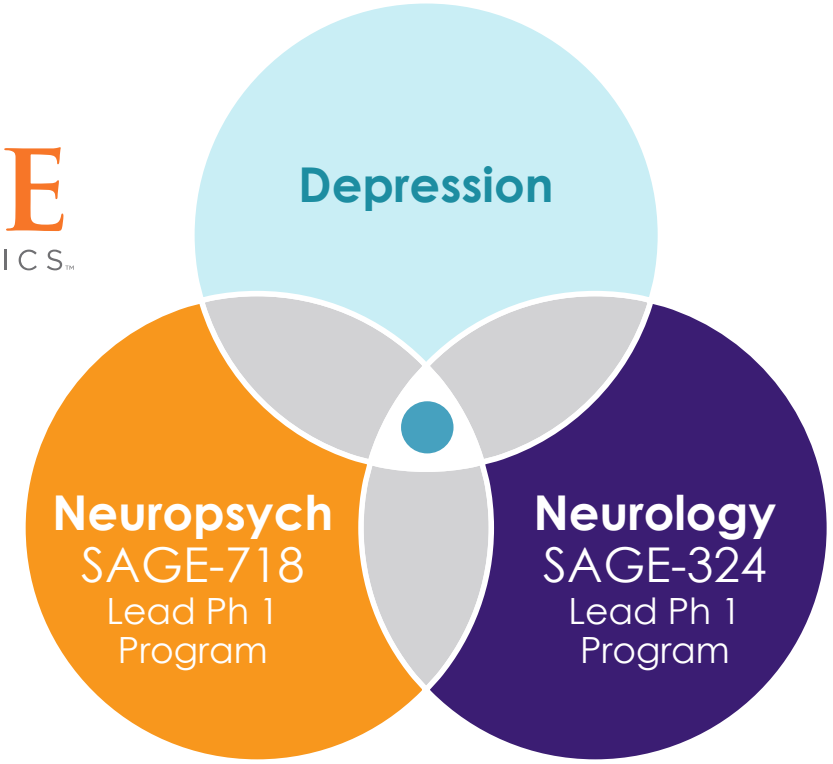
Psychiatry as Medicine



Substantial Portfolio Franchise Opportunities

SAGE THERAPEUTICS

- 1st-in-class Oxysterol-based NMDAr modulator
- Strong preclinical basis for role of NMDA receptor system in cognition
- Multiple diseases associated with low NMDA function
- Initiated Phase 1 Huntington's Disease cohort



- Ongoing Phase 1 program
- Potent anti-seizure preclinical data
- Mechanistic POC in essential tremor
- Targeting essential tremor and epileptiform disorders as lead clinical programs

Advancing a Leading CNS Clinical Portfolio

	COMPOUND	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGISTRATION
Depression	**ZULRESSO™** (brexanolone) Injection	Postpartum Depression					
	SAGE-217	Major Depressive Disorder					
		Postpartum Depression					
		Bipolar Depression					
		Insomnia					
	Undisclosed						
Neurology	**SAGE-324**	Essential Tremor					
		Epileptiform Disorders					
		Parkinson's Disease					
	Undisclosed						
Neuropsych	**SAGE-718**	NMDA Hypofunction/HD					
	Undisclosed						

Significant Milestones Over Next 12-18 Months

FRANCHISE	PROGRAM	ANTICIPATED MILESTONE
DEPRESSION	ZULRESSO	PPD PDUFA target date (March 19th)
		PPD commercial launch in U.S., if approved (June)
	SAGE-217	Bipolar depression Phase 2 ARCHWAY Study open-label data (1H 2019)
		MDD Phase 3 MOUNTAIN Study data (2020)
		MDD with co-morbid insomnia Phase 3 RAINFOREST Study data (2020)
		MDD Phase 3 SHORELINE Study open-label treatment-free interval data (2020)
NEUROLOGY	SAGE-324	Phase 1 SAD and MAD data (1H 2019)
		Phase 1 target engagement data (1H 2019)
		Essential tremor Phase 1 cohort data (2H 2019)
NEUROPSYCH	SAGE-718	Phase 1 SAD and MAD data (1H 2019)
		Phase 1 target engagement data (1H 2019)
		Huntington's Disease Phase 1 cohort data (2H 2019)

SAGE THERAPEUTICS

Delivering on *the promise*…

Seeing the brain differently

makes a world of difference.

Strength of Shionogi's Research in CNS Area

Takeshi Shiota, Ph.D.
Senior Vice President
Pharmaceutical Research Division

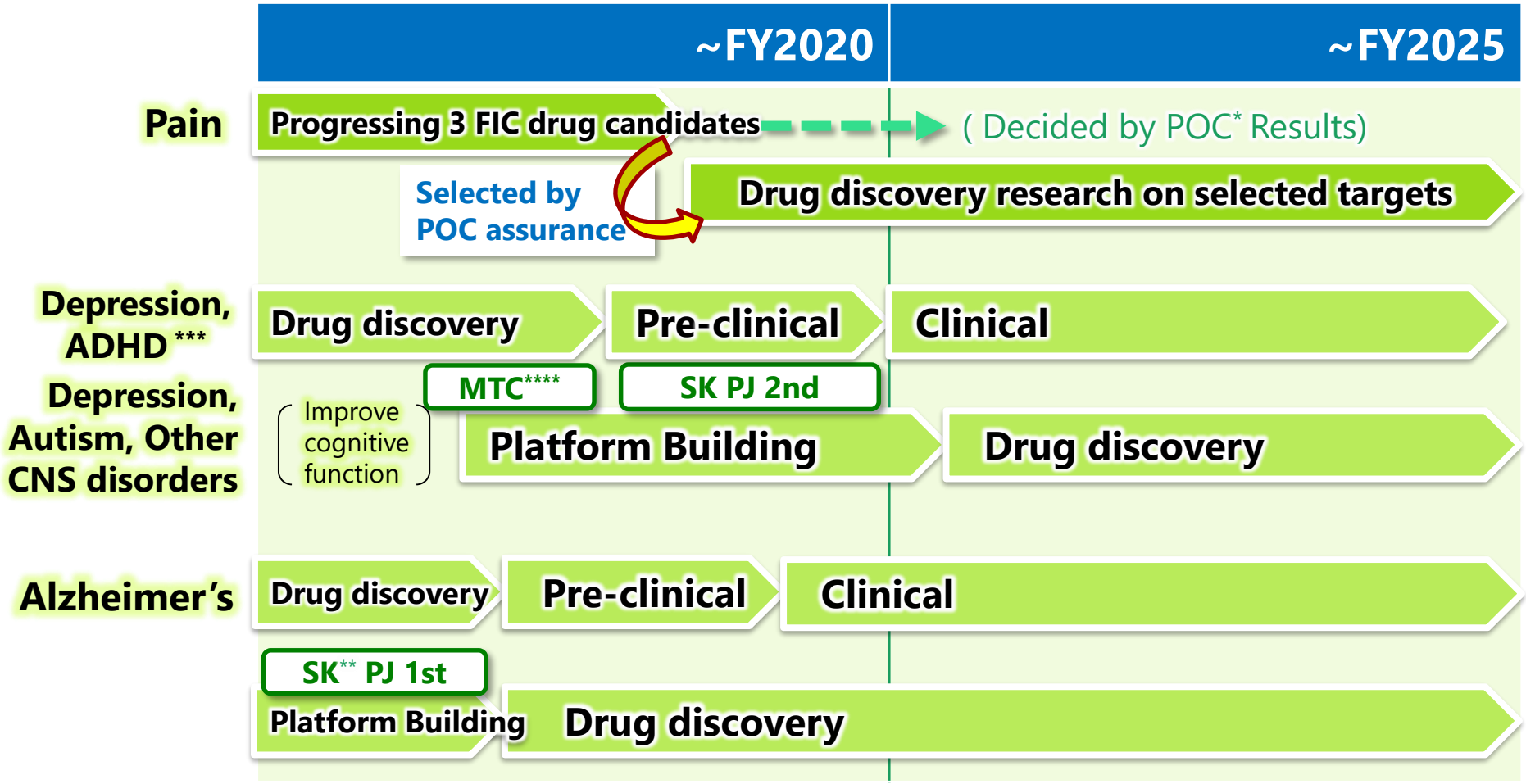
SHIONOGI

Growth Strategy for 2020

Grow sustainably as a drug discovery-based pharmaceutical company contributing to a more vigorous society through improved healthcare

Region/Area to grow	Keys to grow
Japan/US Development in EU/Asia	**Addressing society's needs**
Infectious disease **Pain/CNS**	**Balance of innovation and health economic efficiency**

Drug Discovery Strategies for Pain and CNS



Pain: Focus on selected drug targets

CNS: Utilizing open-innovation to accelerate novel drug discovery

SHIONOGI

* POC: Proof of concept
** SK: Collaboration project of Shionogi and Kyoto Univ.
*** ADHD: attention deficit/hyperactivity disorder
**** MTC: Milner Therapeutics Consortium

Transformation We'd Like to Achieve in CNS Area

As is

Subjective diagnosis

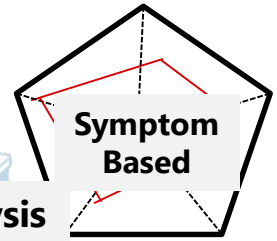
Try & Error of therapy options

Low efficacy

To be

Simple diagnosis

Objective diagnosis based on mechanism



Nerve function analysis

Function improvement

Taylor-made medicines

Non-drug therapy

Very high efficacy
-health economics
-labor productivity

Toward new-generation medicines

Our Efforts Toward the Transformation

SONG for you!

As is

There are various symptoms even in the same disease. However, there is no medication based on working mechanisms of the brain.

Iss-ues

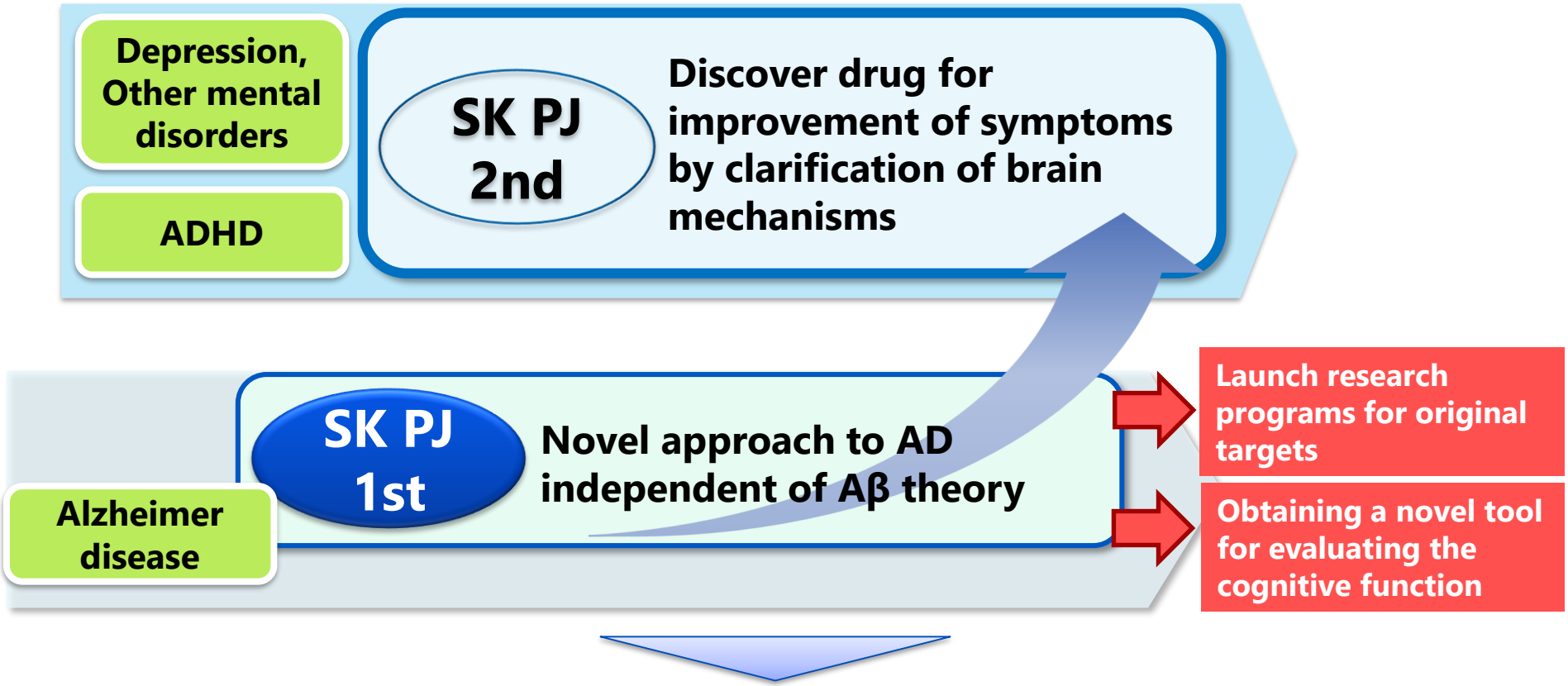
Diagnosis/stratifica-tion of patients by biomarker	Research based on the mechanism in the brain	Appropriate therapy options
•Development of biomarker in order to diagnose and stratify patients	•Development of evaluation index and device in common with human and animals •Development of non-clinical evaluation based on clinical symptoms and brain mechanism	•Research of non-drug therapy •Acquisition of new therapy concept (ex; digital medicine) •Research of brain delivery

Achievement of diagnosis/stratification of patients by biomarker, delivering appropriate therapy options and research of evaluation based on clinical symptoms and brain mechanism

Constructing Research Foundation in CNS Area Through Collaboration

SONG for you!

Ex. SK project (Shionogi-Kyoto Univ.)

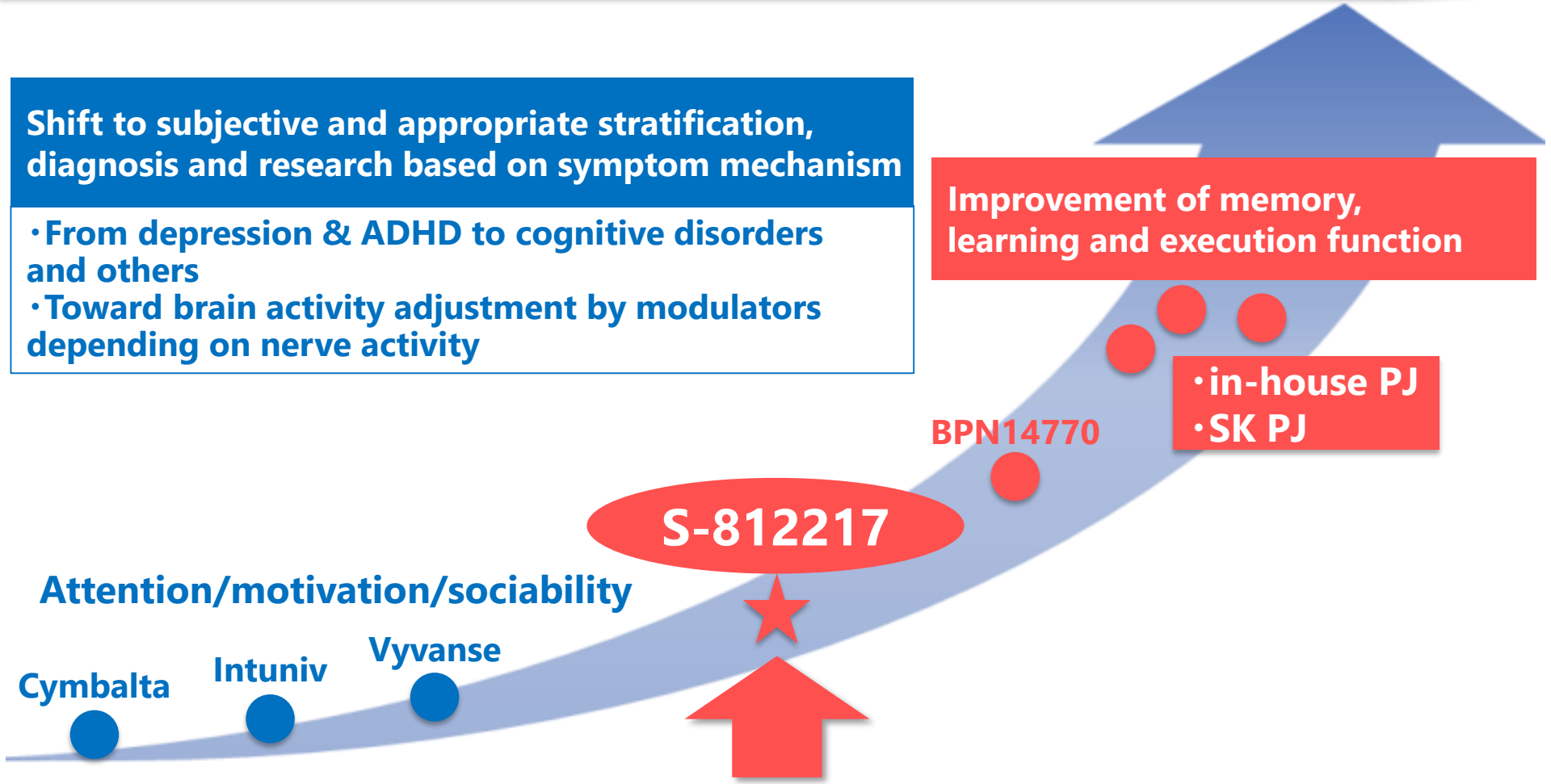


Discover novel drugs to improve symptoms based on deep mechanistic understanding of the disorders

Shionogi's Vision in CNS Area

Shift to subjective and appropriate stratification, diagnosis and research based on symptom mechanism

- From depression & ADHD to cognitive disorders and others
- Toward brain activity adjustment by modulators depending on nerve activity



Based on monoamine hypothesis → **Brain activity adjustment based on nerve activity** → Brain activity adjustment based on symptoms' mechanism

Maximizing the Value of S-812217

S-812217

Pharmacological research

- Accumulate pharmacological evidences
- Expand indications
- Characterize S-812217 by researches for stratifying diseases
- Obtain data about patients who shows high efficacy

CMC research

- Strive for producing a safer drug with higher convenience by researches on formulation

Maximize the value of S-812217 as a next-generation antidepressant by supporting the development in Japan

Development of S-812217 in Japan

Jun Yoshimoto D.V.M., Ph.D.
Vice President
Project Management Department
Global Development Division

SHIONOGI

Social Impact of Depression in Japan

Antidepressant market & work productivity loss due to depression

5M Patients

- Ca. **5M patients** with depression in Japan[1)]
  - The largest population among non-fetal diseases
- Current antidepressant market in Japan : Ca. **160 B yen**: Cymbalta® keeps top-share

160 B yen Market

40M days/year & 400 B yen losses

- Absence from work for **40M days/year** in total
- Work productivity loss equivalent to ca. **40 B yen** [2,3)]
  - The biggest impact among all diseases

Major unmet medical needs for currently available therapy

Insufficient Efficacy

- Remission rate after the first treatment using SSRI[4)]: 36.8%[5)]
- Cumulative remission rate after changing anti-depressants up to 3 times[6)]: ca. 67% in total[5)]

Slow Onset

- 2-8 weeks are needed for efficacy onset
- Prolonged debilitation and increased risks of deterioration or suicide due to slow onset[7)]

Complicated regimen

- Dose adjustment is necessary for mitigating adverse events

1) WHO, Depression and Other Common Mental Disorders Global Health Estimates, 2) Collins JJ, et al. J Occup Environ Med 2005; 47, 3) Norito Kawakami. Health Labor Sciences Research Grant Research on Psychiatric and Neurological Diseases and Mental Health from FY2004 to FY2006. 2007; 200632010B: 1-21, 4) QIDS-C_{16} Score<= 5, 5) Am J Psychiatry 2006; 163:1905–1917, 6) SSRI,SNRI,Nassa, Therapeutic algorithm based on guidelines for treatment by tricyclic antidepressant drugs, 7) JAMA. 2004;292:338-343

Profile of S-812217

	SSRI/SNRI/NaSSA - First-line antidepressants -	S-812217
Mechanism of Action	Increase of monoamine (serotonin, noradrenaline)	Positively modulate $GABA_A$ receptor
Dosing Schedule	Dose adjustment is necessary for mitigating adverse events	Once-daily fixed dosage for 14 days
Efficacy	Efficacy on anxiety and motivation	Raid onset, greater and durable effect
Onset	Over 2 weeks until onset	Rapid onset of efficacy in 24 hours
Power	Remission rate after 6-week treatment: 36.8%[1)]	• Remission rate at 2-week treatment completion: 64.3%[2)] • Efficacy on broad symptoms including core ones
Sustainability	No data about sustainability	Durable effect even in drug holidays
Adverse events	Nausea, dry mouth, constipation	somnolence

Meet unmet needs for the current treatment

1) Am J Psychiatry 2006; 163:1905–1917
2) Phase II study for major depressive disorder

Concept for S-812217 Development

1. Novel antidepressant candidate following Cymbalta®

- Contribute to sales beyond 2020 by launching novel drugs in CNS area continuously

2. Breakthrough profiles

- **Rapid onset:** in 24 hours of the first dosing
- **Greater efficacy:** superior to currently available antidepressants
- **Durable efficacy:** following treatment discontinuation
- **Better medication adherence:** No need of dose adjustment including titration and tapering, once daily dosing for 14 days

3. Maximize values by amassing new evidence

- Functioning, work performance and productivity effects[1,2,3,4)]
- Health economic evaluation including HTA (Health Technology Assessment)

Provide new values with depression treatments

1) Wagner S, J Psychiatr Res 2017; 94: 96-106., 2) Szegedi A, Jansen WT, J Clin Psychiatry 2009; 70: 344-53., 3) Sarfati D, Ann Clin Psychiatry 2017; 29: 11-16., 4) Sheehan DV, J Affect Disord 2017; 24: 299-313,

Target of S-812217 Positioning

1. First-line antidepressant

- **Target profiles: achieve remission of depression by short-term treatment**
  1. Simple regimen
  2. Efficacy on broad symptoms
     - ✓ Efficacy on core symptoms (Deppressed mood and retardation)
  3. Rapid and greater efficacy
  4. Good tolerance and safety

2. Antidepressant for broad depression symptoms

- **Efficacy on patients with severe symptoms, in acute stage, or not responding to currently available therapy**

Effective to broader depressant symptoms

Development of S-812217 in Japan

Phase I study in Japan - ongoing
- Check difference in race

- Phase I study is proceeding steadily
- S-812217 is well-tolerated and show similar safety profiles to those in the U.S. clinical studies so far

Clinical study in patients - plan to initiate in FY2019
- Optimize clinical study package

- Indication: Depression
- Regimen: Once-daily fixed dosage for 14 days

Proceed development of S-812217 rapidly with our high expertise in development in Japan

- **Utilize data from clinical studies conducted by SAGE and priority review system**
- **Proceed development in Taiwan and South Korea based on data from clinical studies in the U.S. and Japan**

Q&A

Forward-Looking Statements

- Forecast or target figures in this material are neither official forecasts of earnings and dividends nor guarantee of target, achievement and forecasts, but present the midterm strategies, goals and visions. Official earnings guidance should be referred to in the disclosure of the annual financial report (*kessan tanshin*) in accordance with the rules set by Tokyo Stock Exchange.
- Materials and information provided during this presentation may contain so-called "forward-looking statements". These statements are based on current expectations, forecasts and assumptions that are subject to risks and uncertainties which could cause actual outcomes and results to differ materially from these statements.
- Risks and uncertainties include general industry and market conditions, and general domestic and international economic conditions such as interest rate and currency exchange fluctuations. Risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, technological advances and patents attained by competitors; challenges inherent in new product development, including completion of clinical trials; claims and concerns about product safety and efficacy; regulatory agency's examination period, obtaining regulatory approvals; domestic and foreign healthcare reforms; trend toward managed care and healthcare cost containment; and governmental laws and regulations affecting domestic and foreign operations.
- For products that are approved, there are manufacturing and marketing risks and uncertainties, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials, and failure to gain market acceptance.
- Shionogi disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.
- This material is presented to inform stakeholders of the views of Shionogi's management but should not be relied on solely in making investment and other decisions.
- You should rely on your own independent examination of us before investing in any securities issued by our company. Shionogi shall accept no responsibility or liability for damage or loss caused by any error, inaccuracy, misunderstanding or changes of target figures or any other use of this material.
- This English presentation was translated from the original Japanese version. In the event of any inconsistency between the statements in the two versions, the statements in the Japanese version shall prevail.