

# Depression Rising (Again): Turning the Corner in Psychiatry's Most Burdensome Disorder

Joel Sandler, Ph.D.  
Associate Principal,  
Defined Health

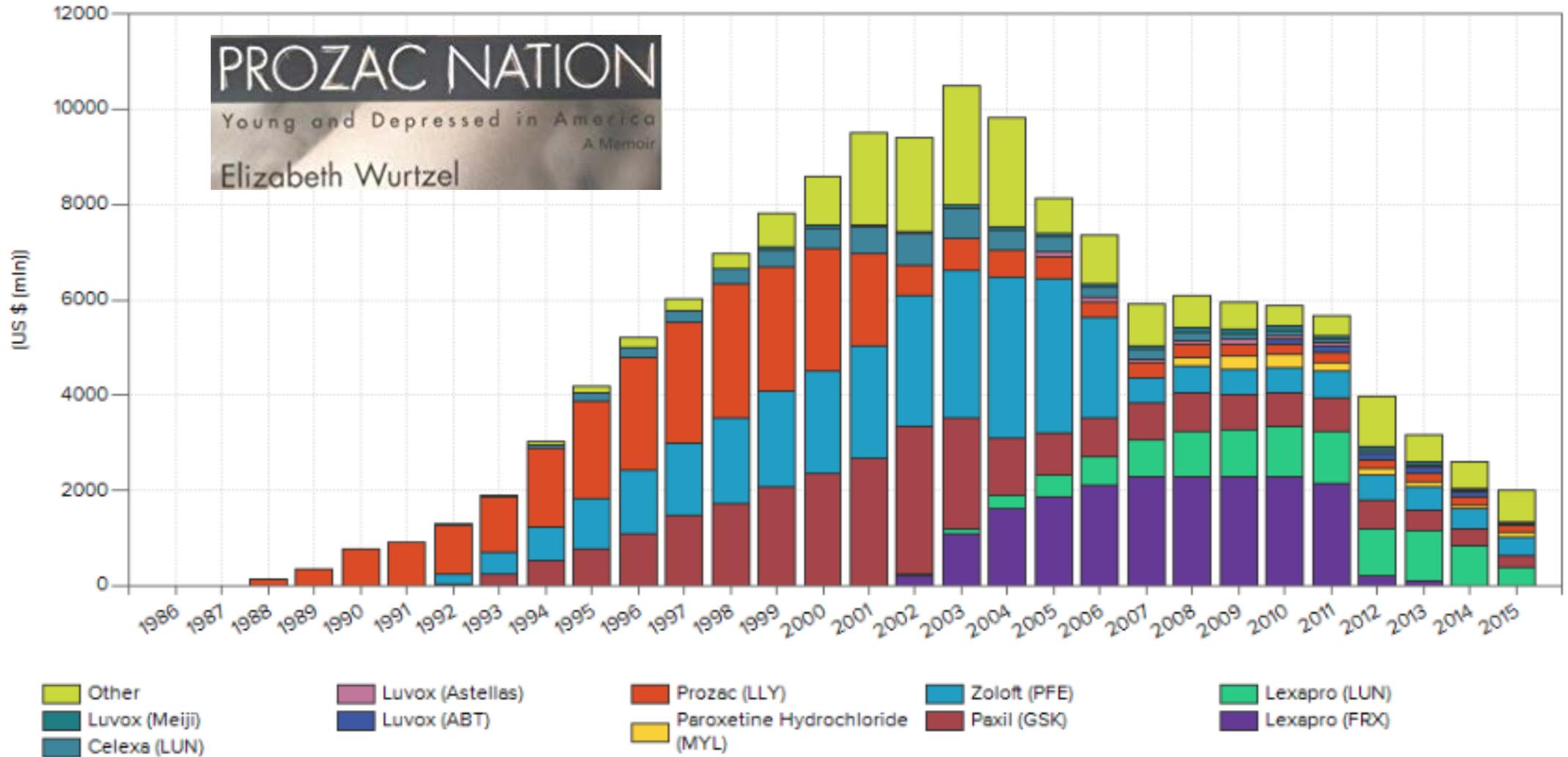
Harry Tracy, Ph.D.  
Founder and President,  
NI Research

Roger Longman  
Chief Executive Officer,  
Real Endpoints

***Defined Health Insight Series Briefing***  
**June 18, 2018**

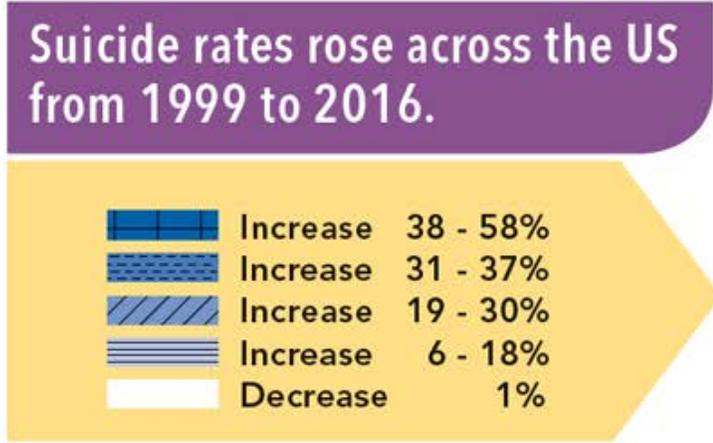


# SSRIs: The Rise and Fall (i.e. Genericization) of an Empire

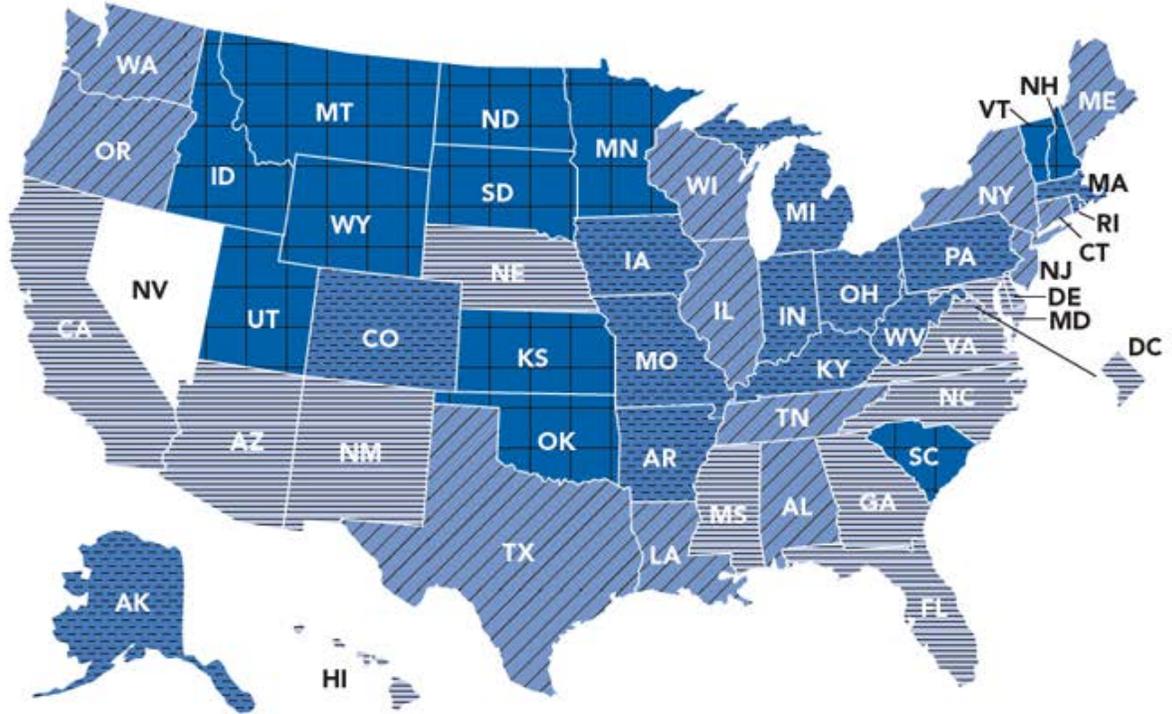


EvaluatePharma

# And Yet the Problem Intensifies

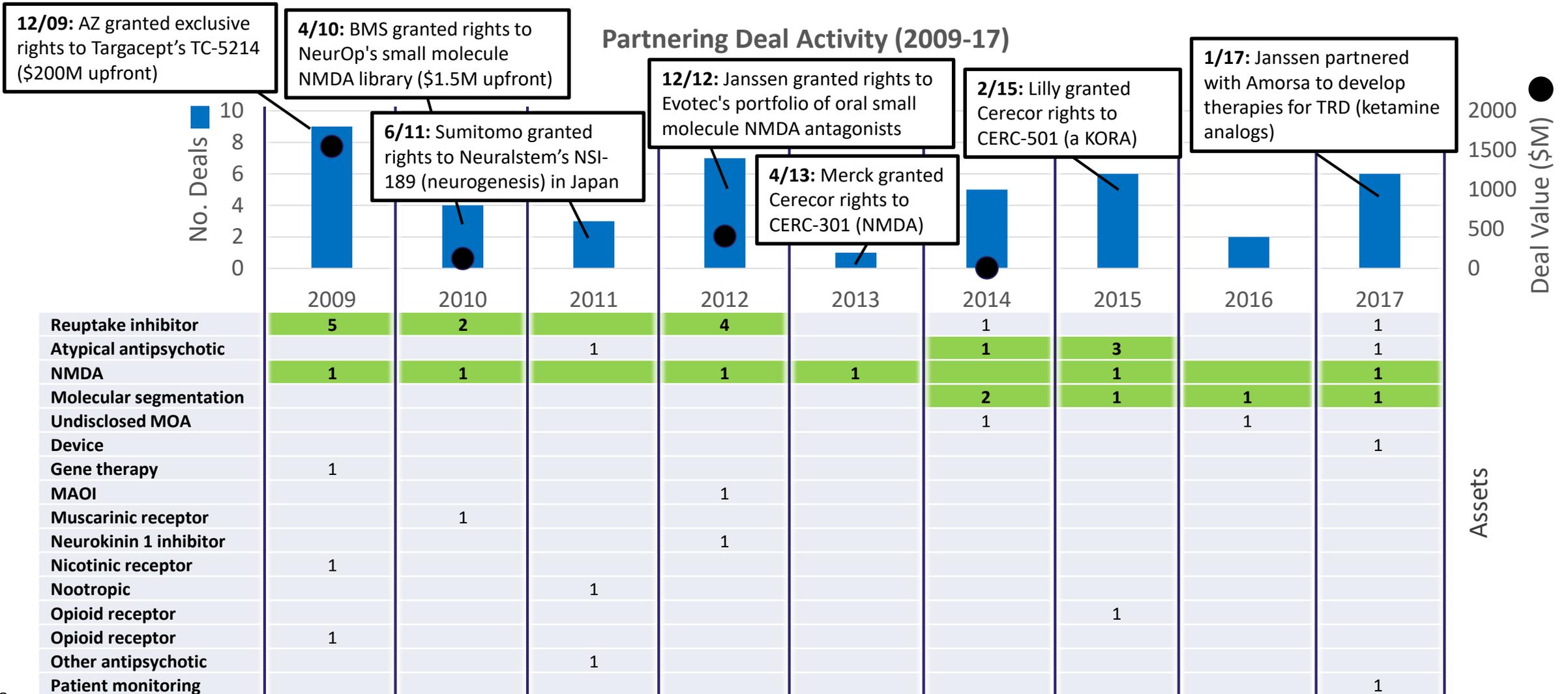


SOURCE: CDC's National Vital Statistics System; CDC Vital Signs, June 2018.



Suicide rates have been rising in nearly every state, according to the latest Vital Signs report by the Centers for Disease Control and Prevention (CDC). **In 2016, nearly 45,000 Americans age 10 or older died by suicide.** Suicide is the 10th leading cause of death and is one of just three leading causes that are on the rise.

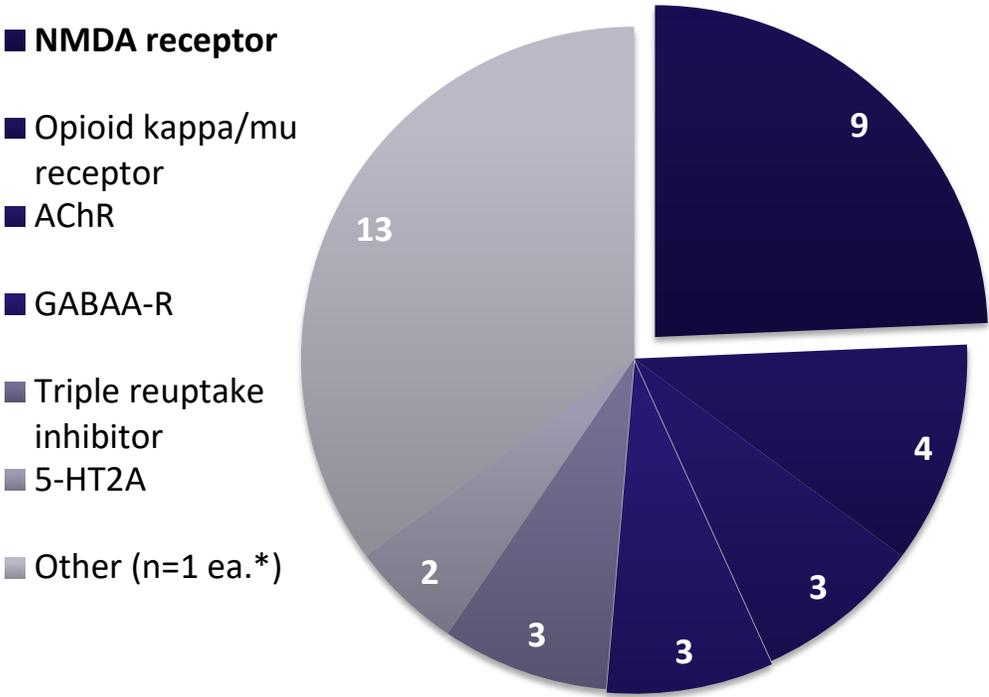
# Partnering Activity Remains Tepid at Best



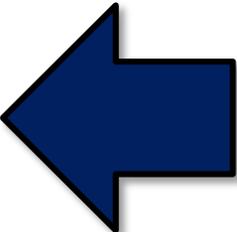
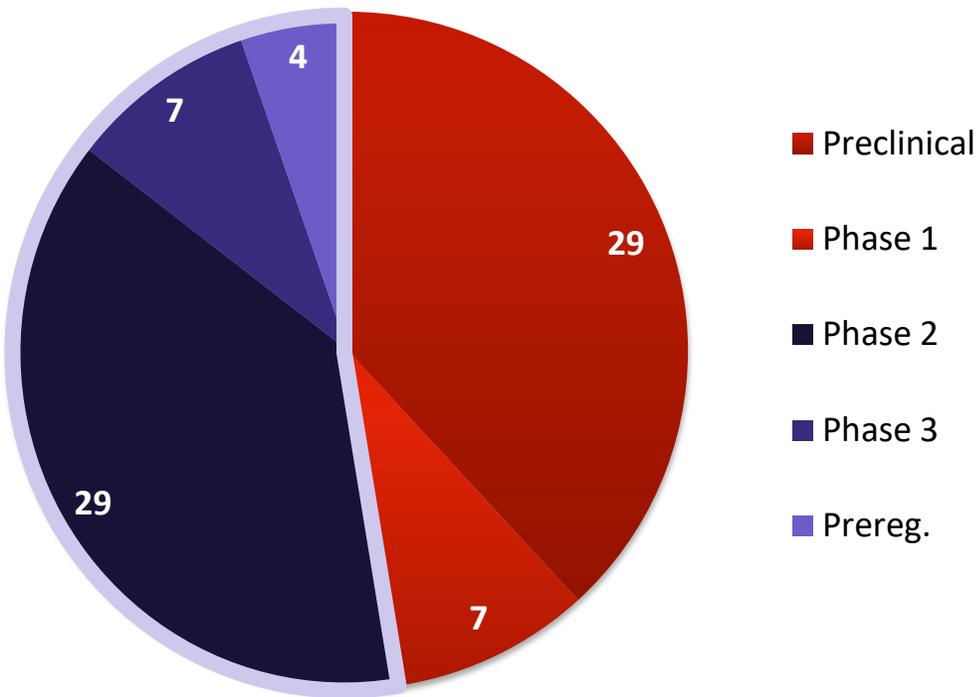
BCIQ

# NMDA Modulators Well-Represented in Late-Stage Pipeline

**Phase 2-Registration Depression Pipeline by Target (n = 40)**



**US Depression Clinical Development Pipeline by Phase (n = 76)**



Adis, Cortellis

\*n-of-1 targets include: SSRI + 5-HT1A, 5-HT1A, 5-HT7, D2/D3 receptor, D2/D3 + 5-HT1A/2A, IL-6, mGluR5, NET, Neuronal growth factor receptor, Chemosensory receptors, NOPR, Orexin-2, SSRI

# The New Crop of Antidepressants?

Emerging Programs	Allergan	Sage Therapeutics		Marinus	Janssen
	Rapastinel	Brexanolone	SAGE-217	Ganaxolone	Esketamine
Dev. Phase	3	Pre-reg	2	2	3
Exp. Entry Date	2020	2018/2019	2020	2021	2019
Indication(s)	TRD	PPD	MDD, PPD	PPD	TRD
MOA	NMDA partial agonist	GABA A receptor modulator	GABA A receptor modulator	GABA A receptor modulator	NMDA receptor antagonist
ROA	IV	IV	Oral	IV, Oral	Intranasal
Comments	Rapid effect; pivotal data due 1H2019; oral program in-licensed	Rapid effect; valuation largely based on next-gen oral analog ('217)	Rapid effect; expedited development plan announced by FDA	Top-line PPD data for IV and oral formulations expected later this year	Marginal but significant improvement vs. placebo

## COLLABORATIONS, DEALS

**Allergan doubles down on NMDA depression drug development efforts, bagging an option to a small molecule followup drug**



by JOHN CARROLL — on May 22, 2018 08:46 AM EDT

Updated: 08:54 AM

## FDA, REGULATORY

**With a big assist from the FDA, Sage plots a swift march through PhIII for oral depression drug — market cap swells \$1B-plus**



by JOHN CARROLL — on June 12, 2018 07:34 AM EDT

Updated: 01:21 PM

## RESULTS

**J&J racks up a fresh set of positive pivotal data for depression drug esketamine — but questions linger on safety**

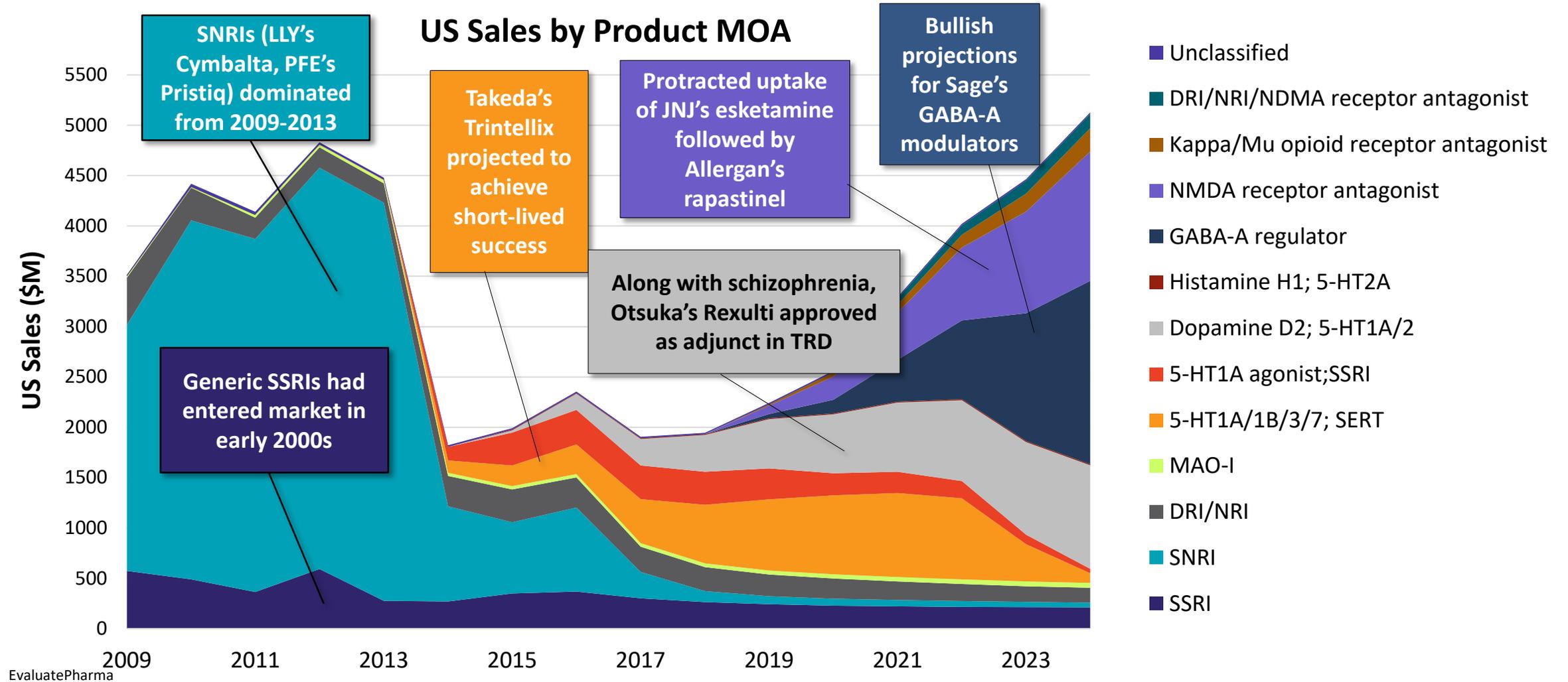


by JOHN CARROLL — on May 31, 2018 01:49 PM EDT

Updated: 01:58 PM

Adis, Cortellis, company press releases

# Succession (and Modest Diversification) on the Horizon



# Rollercoaster Rides – Sage’s Valuation Largely Driven by Performance of Oral ‘217

SAGE Therapeutics, Inc. (SAGE:NASDAQ) Market Summary



Yahoo Finance, company press releases

# Rollercoaster Rides – FDA Now Willing to Review Alkermes’ Opioid Receptor Modulator



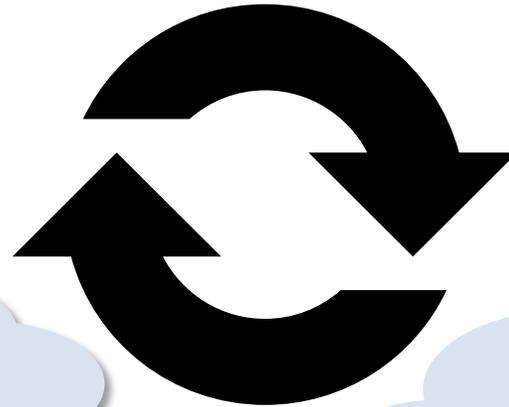
# Towards a Tipping Point in Depression?



Will regulatory and commercial success catalyze further enthusiasm, investment?

“The risk associated with CNS drug development broadly is considered too great as commercial risk is added to the inherent scientific and clinical development risk associated with neuropsychiatric disease.”

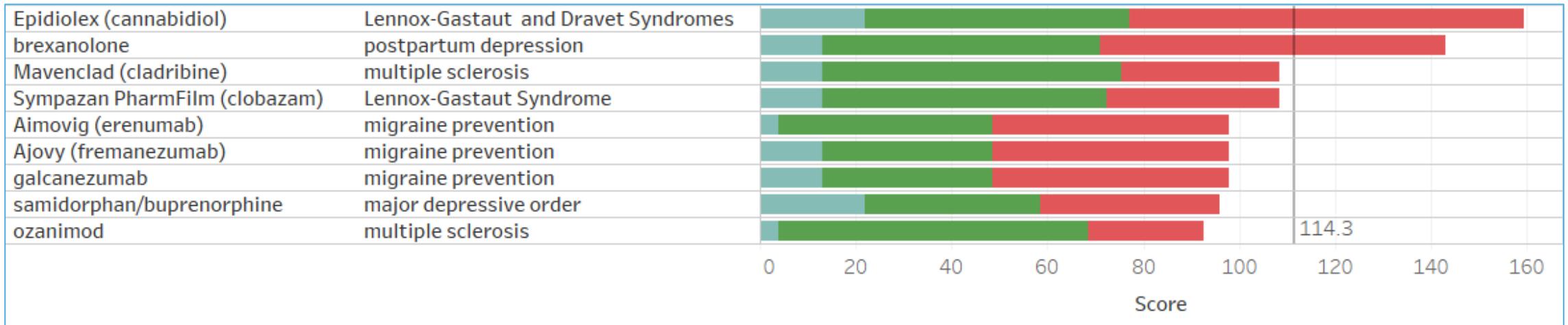
- GS Johnson, Neurobiol Dis. 2014



Are emerging clinical candidates adequately positioned to address unmet needs?

Remaining gaps, opportunities for innovators, partners, investors?

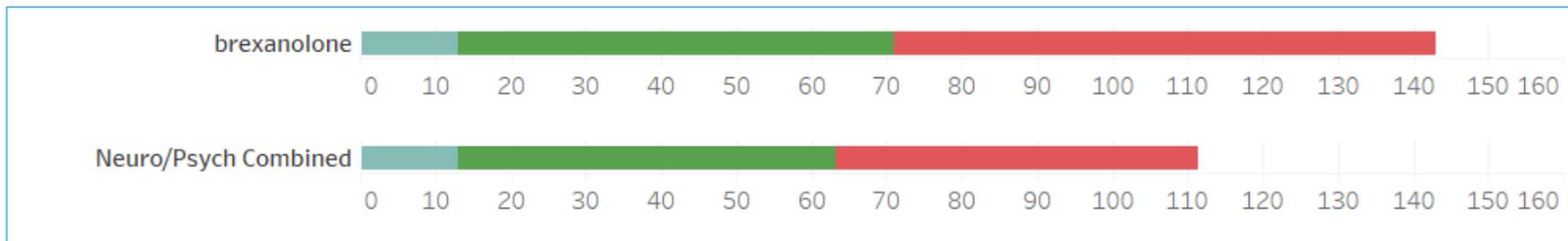
# As a class, 2018 neuro drugs will face not insignificant access challenges



Average of 114.3 calculated from all 2018 launches/likely launches scored



# Brexanolone from a payer's point of view



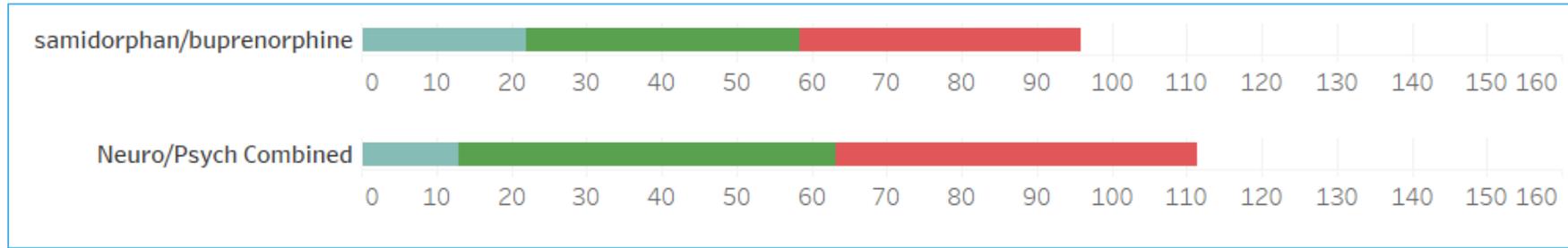
## Access Advantages

- Treats high unmet need
- Limited therapy duration
- FDA breakthrough status
- Medical benefit drug
- Effective patient advocacy organizations in category

## Access Challenges

- New payer-expense category
- Undefined volume of use
- Off-label potential: label and evidence uncertainty re. moderate PPD
- Durability of effect given 30-day endpoint

# Samidorphan/buprenorphine from a payer's point of view



## Access Advantages

- Protected class
- Novel mechanism
- Serious disease
- Superiority data vs competitive agents

## Access Challenges

- Many generic "step-throughs"
- Mixed trial results
- Limited bundling advantage vs competitors
- If pricing high, patient cost-sharing challenges in Medicare