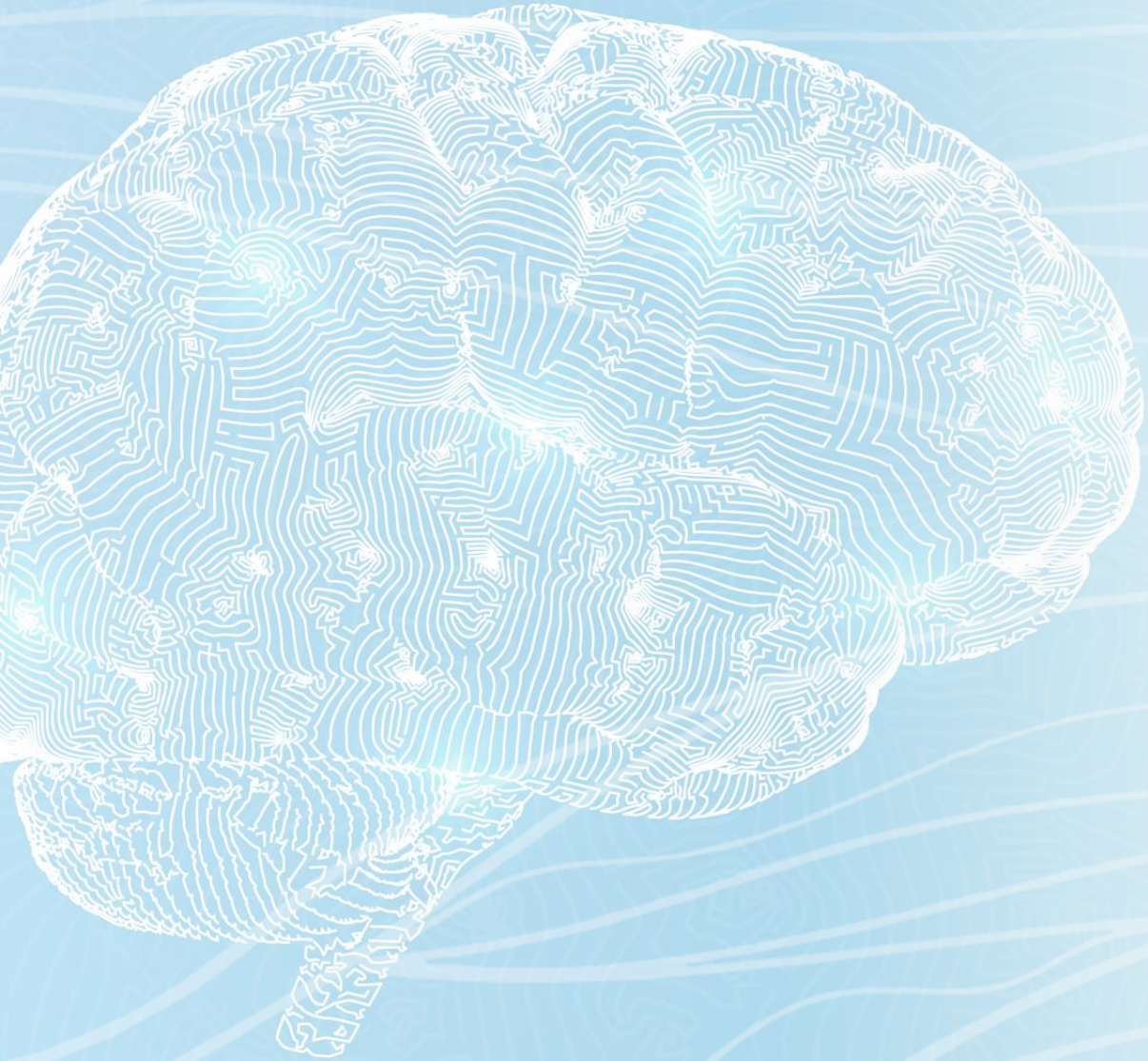

KARUNA
THERAPEUTICS

Developing novel therapies with the potential to transform the lives of people with disabling and potentially fatal neuropsychiatric disorders and pain

JANUARY 2020

Legal disclaimer

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Karuna at-a-glance

KarXT

- **KarXT is a novel mechanism of action therapeutic** targeting CNS indications representing large and underserved patient populations
- **KarXT met primary endpoint in Phase 2 clinical trial** in patients with acute psychosis in schizophrenia demonstrating a statistically significant ($p<0.0001$) and clinically meaningful 11.6 point improvement on PANSS total score baseline vs. placebo
- **KarXT was generally well tolerated without the burden of common side effects** of currently marketed antipsychotics

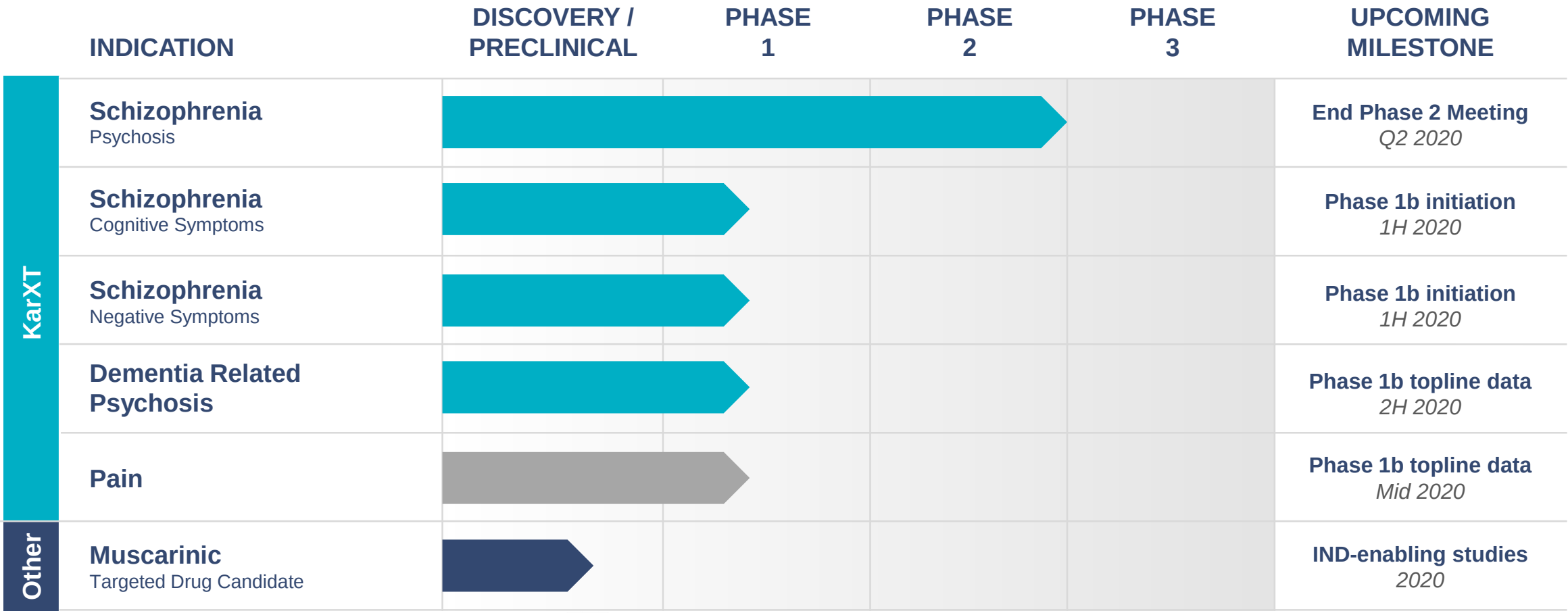
Pipeline-in-a-Product

- **End-of-Phase 2 meeting expected in Q2 2020 with Phase 3 initiation expected by the end of 2020** for the treatment of psychosis in schizophrenia
- **Near term development** opportunities
  - ✓ Negative and cognitive symptoms of schizophrenia
  - ✓ Dementia Related Psychosis, including in Alzheimer's disease
  - ✓ Pain
- **Advanced formulation development** underway to optimize therapeutic window and improve compliance

Experienced Team

- **Leadership with proven expertise** in CNS drug development and commercialization
- **Advised by world experts** in schizophrenia, Alzheimer's disease, and neuroscience
- **Seasoned board of directors** and blue-chip biotech investors

Karuna's portfolio of muscarinic receptor-targeted programs



Leadership team with deep expertise in neuroscience and drug development

Steve Paul, M.D. | Chairman and CEO

Former EVP and president at Eli Lilly Research Labs; Co-founder, board member at Sage Therapeutics & Voyager Therapeutics; Former scientific director of NIMH

Andrew Miller, Ph.D. | Founder and COO

Founder and inventor of KarXT technology; Former VP at PureTech; 40 under 40 innovators award from MedTech Boston; Director and Former COO at Entrega

Stephen Brannan, M.D. | CMO

Former Therapeutic Head of Neuroscience at Takeda; senior positions at Novartis (Exelon patch), Eli Lilly (Cymbalta), Cyberonics, & Forum Pharmaceuticals

Troy Ignelzi | CFO

Former CFO at scPharmaceuticals and Juventas; Finance, BD, operations and sales executive at Esperion Therapeutics, Insys Therapeutics and Eli Lilly

Alan Breier, M.D. | Chief Clinical Adviser

Chair, Karuna Scientific Advisory Board; Senior Professor of Psychiatry, Indiana University Mental Health Research and Education; Vice-Chair for Clinical Research

Greg Brophy, Ph.D. | Senior Adviser, Regulatory

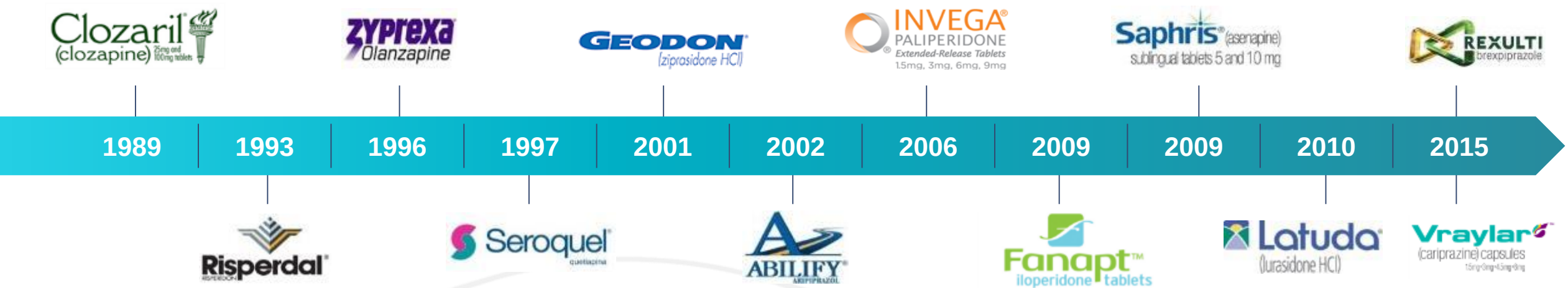
Former Senior Head of Neuroscience Regulatory at Eli Lilly; Former executive leader of regulatory (consulting) at Acadia

David Hewitt, M.D. | SVP, Medical

Former CMO, Syneos Health and inVentiv Health; Former Executive Director at Merck; Former Senior Director Ortho-McNeil and Johnson & Johnson

Antipsychotics: Blockbuster sales, but little innovation

- Today's drugs rely on **same mechanism as drugs of the 1950s** (first antipsychotic drug, chlorpromazine, discovered in 1952)
- Sales of antipsychotic drugs were **>$11B in 2015** and are expected to be **>$14B by 2025 worldwide**
- Despite limited efficacy, severe side effects, and the availability of generic medicines, antipsychotic drugs such as Zyprexa, Seroquel and Abilify each achieved **>$5B peak sales worldwide**
- Antipsychotics are a **protected Medicare Part D class**



Unmet need. Significant opportunity.

Schizophrenia

- Positive (psychosis), negative and cognitive symptom domains
- Antipsychotics currently approved only to treat psychosis and offer modest efficacy in many patients; nothing to treat negative and cognitive symptoms
- Significant side effects including movement disorders, weight gain, sedation, etc.
- >21 million patients with schizophrenia worldwide with ~2.7m in the US

Dementia Related Psychosis

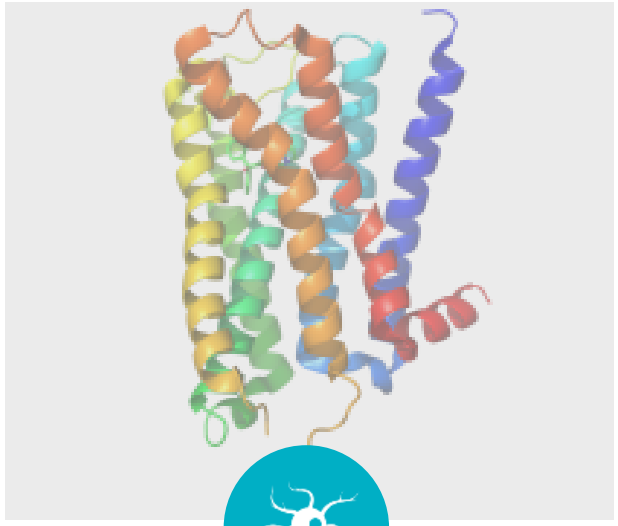
- Antipsychotics prescribed despite black box warning for increased morbidity and mortality
- No approved medicines for treatment of psychosis in Alzheimer's disease, the largest underlying cause of DRP
- Psychosis afflicts up to 50% of AD patients; 5.8m AD patients in the US

Pain

- Multiple opportunities across different pain modalities: acute (post-op), inflammatory, and neuropathic
- Reducing or eliminating opioid use is major public health need

The Rationale for KarXT

Unrealized potential of muscarinic receptors



Muscarinic receptors in the brain are promising targets for schizophrenia, dementia related psychosis, and pain

Many companies pursued muscarinic drug development, but were stymied by side effects caused by peripheral muscarinic receptors

A novel approach is needed to realize potential of muscarinic agonists

Our proprietary lead product candidate: KarXT

xanomeline
(muscarinic *agonist*)

- Human PoC in double-blind, placebo-controlled trials in schizophrenia and Alzheimer's
- Trials enrolled over 800 patients including 68 patients for ≥ 1year
- Exclusively licensed from Eli Lilly

KarXT

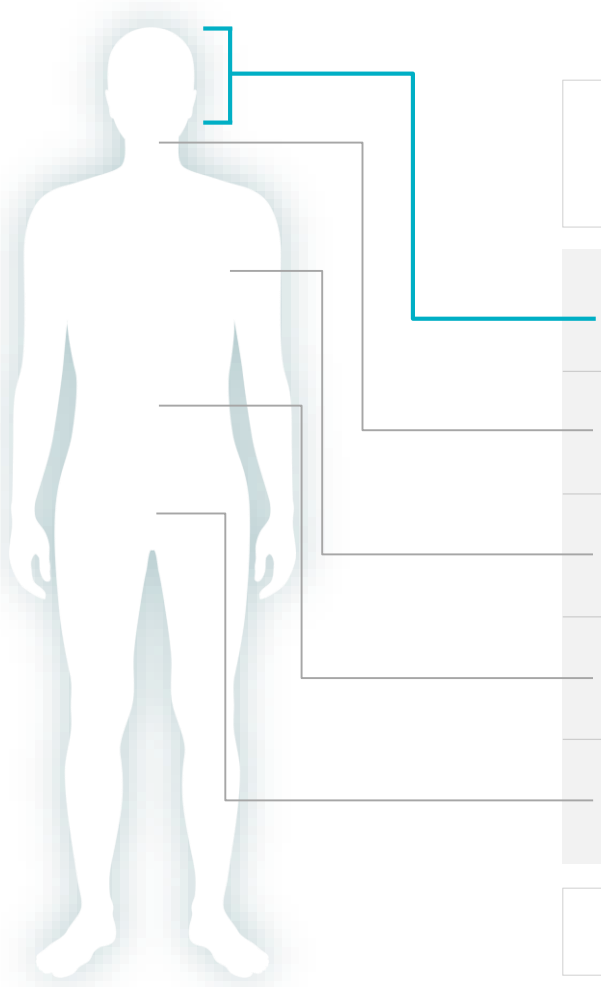
xanomeline + trospium chloride

KarXT is designed to maintain efficacy of xanomeline while ameliorating its cholinergic AEs

trospium chloride
(muscarinic *antagonist*)

- Does not meaningfully cross the blood brain barrier, limiting effects to peripheral tissues
- No known metabolic overlap with xanomeline
- Generic drug for overactive bladder used since the 1960s

KarXT selectively activates muscarinic receptors in the brain



System	Potential Impact on Symptoms xanomeline + trospium = KarXT			Commentary
Central Nervous System	↑	N/A	↑	Improvement in psychosis and cognition
Salivation Glands	↑	↓	—	Tolerability from neutralization of peripheral activation
Sweat Glands	↑	↓	—	
GI Tract	↑	↓	—	
Bladder	↑	↓	—	

↑ Increase Activity | ↓ Decrease Activity | — Offsetting Effect

Schizophrenia

THE UNMET NEED

- Chronic, disabling disorder typically diagnosed in late teenage years or early adulthood
- Characterized by recurring episodes of psychosis requiring long-term treatment with antipsychotic drugs in most patients
- Affects over 21 million people worldwide
  - 2.7 million Americans (0.5% -1.0% of U.S. population) had schizophrenia in 2017
- Today's standard of care relies on same mechanism as drugs of the 1950s
- In many patients, approved antipsychotics offer only modest efficacy and significant side effects

THE KarXT OPPORTUNITY

Est. Market	Antipsychotics: >$14B by 2025 worldwide
Treatment Indications	Positive symptoms (psychosis) Negative symptoms Cognitive symptoms
Status	Ph2 Trial Data released 11/19 Met primary, secondary endpoints Final data analysis ongoing
Next Steps	End of Phase 2 Meeting Q2 2020

KarXT Phase 2 Trial Results Analysis

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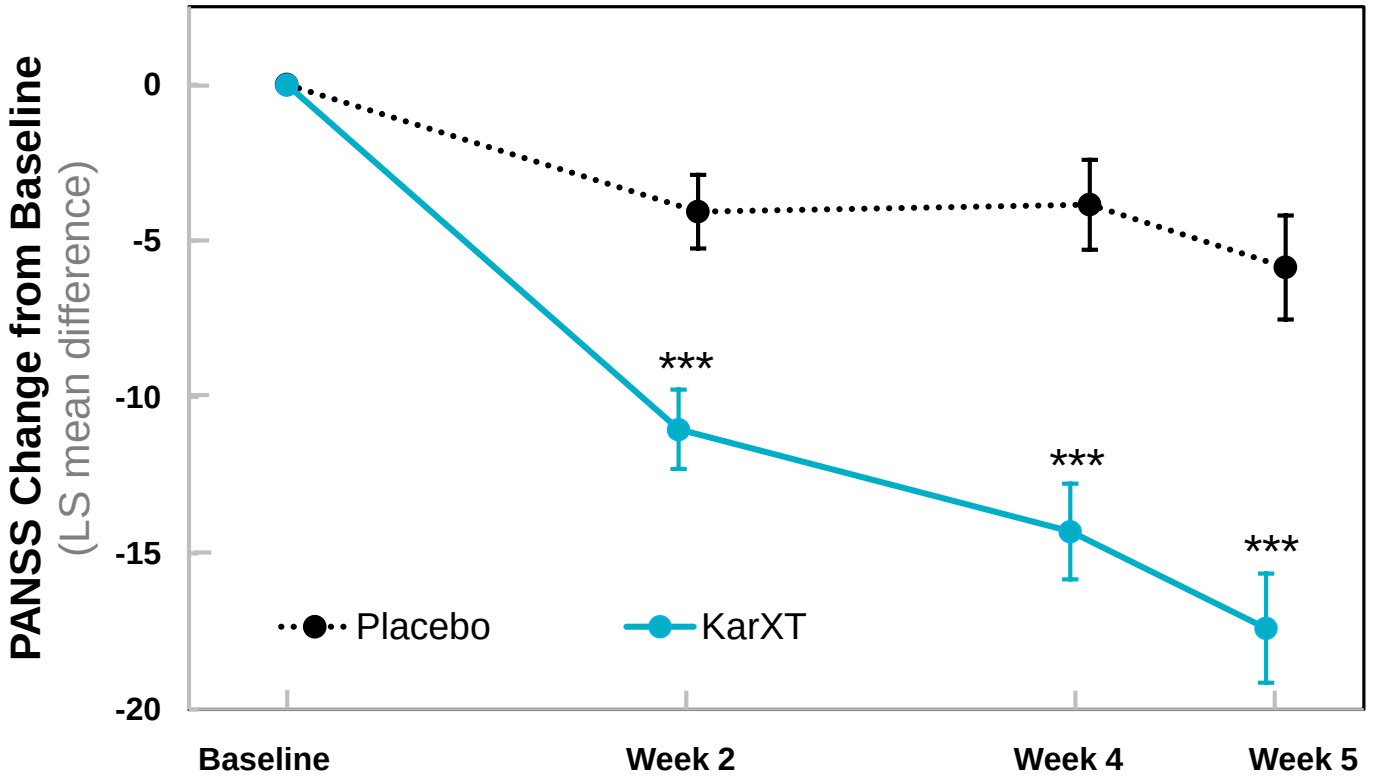
PHARMACEUTICALS

Phase 2 trial design overview

Design:	**Same fundamental trial design and primary endpoint used in pivotal studies to support registration of other antipsychotic drugs**
	• Randomized, double-blind, placebo-controlled, inpatient trial in patients with schizophrenia experiencing acute psychosis
	• 182 patient, two-arm trial with 1:1 randomization to KarXT (N=90) or placebo (N=92) with a five-week treatment period using flexible dose design
	  • **Days 1-2:** 50/20 KarXT BID (50 mg xanomeline/20 mg trospium)
	  • **Days 3-7:** 100/20 KarXT BID
	  • **Days 8-35:** 100/20 KarXT BID with optional increase to 125/30 KarXT BID; ***titration based only on tolerability***
	• Patients were washed out of any antipsychotic drugs prior to randomization

Key Endpoints:	**Primary endpoint of change in total PANSS from baseline vs. placebo at week 5 in the modified intent to treat population (mITT)** **Secondary endpoints:** PANSS-positive and -negative subscales, CGI, PANSS Marder factor, cognitive battery, and others

Primary endpoint: PANSS total score at week 5



mITT population

***P<0.0001

Clinically meaningful and statistically significant improvement in total PANSS vs. placebo

- 11.6 point improvement at week 5 with p<0.0001 (-17.4 KarXT vs. -5.9 placebo)
- Statistical separation at every assessed time point
- Cohen's d effect size of 0.75

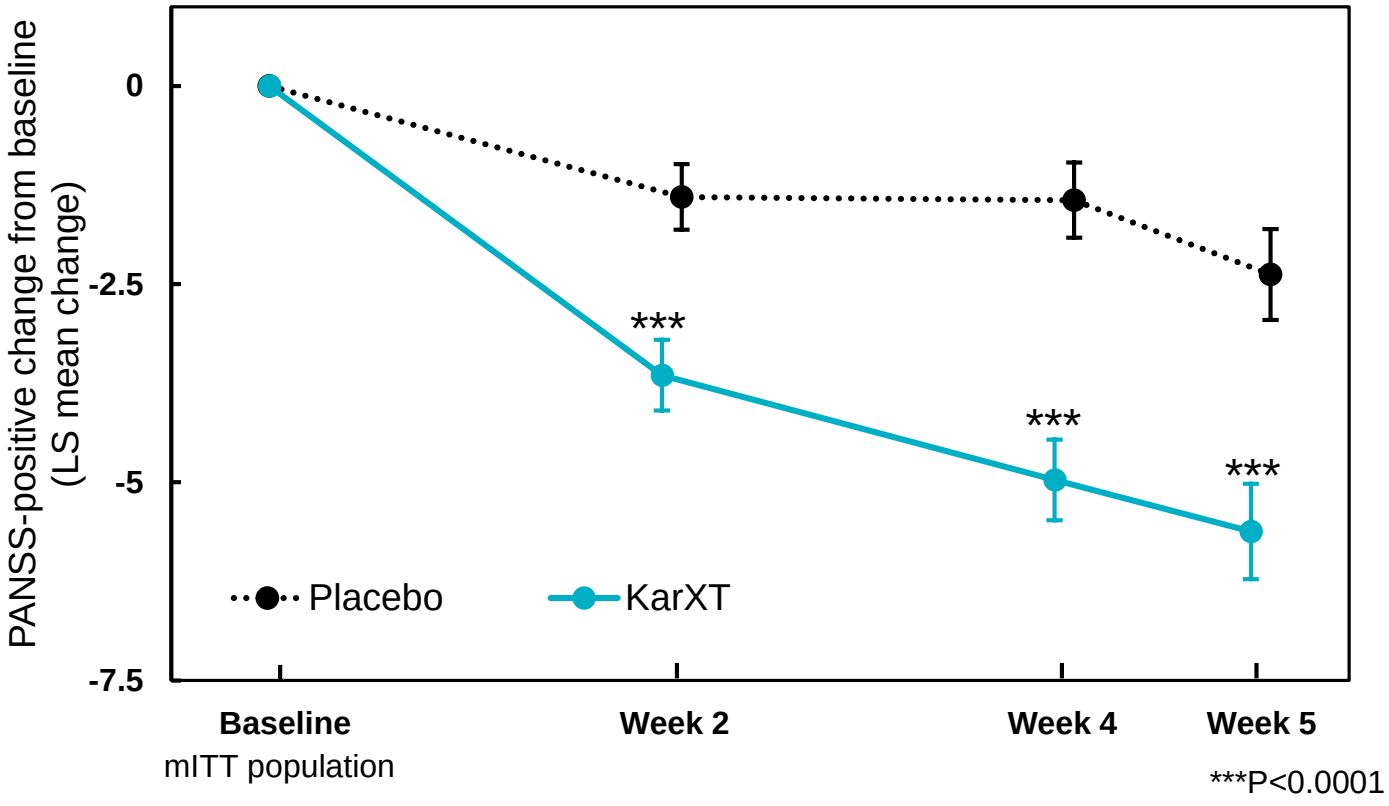
Meta-analysis of Cohen's d effect size

Therapy	COHEN'S d	NUMBER OF STUDIES	NUMBER OF PATIENTS	PEAK SALES	YEAR APPROVED
KarXT	**0.75**	**1**	**182**	**-**	**-**
Risperidone	0.58	15	3,036	>$3b	1993
Olanzapine	0.55	19	3,298	>$5b	1996
Quetiapine	0.43	8	2,140	>$6b	1997
Aripiprazole	0.39	9	1,761	>$9b	2002
Lurasidone	0.35	7	2,043	>$3b	2010

KarXT Phase 2 effect size of 0.75 compares favorably with meta-analysis of current drugs

Leucht et al. 2017 Molecular Psychiatry

Secondary endpoint: PANSS-positive sub-scales



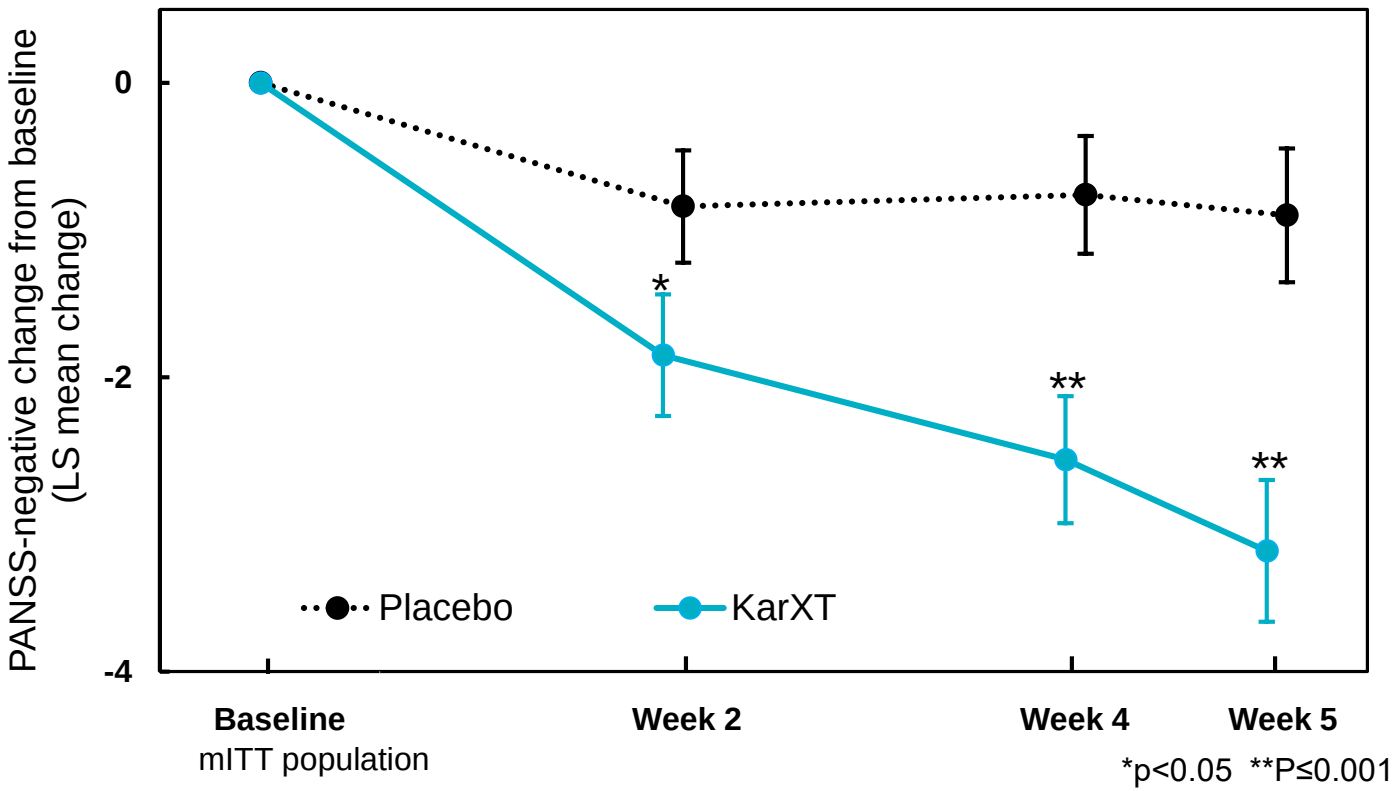
mITT population

***P<0.0001

Clinically meaningful and statistically significant improvement in PANSS positive vs. placebo

- 3.2 point improvement at week 5 with p<0.0001 (-5.6 KarXT vs. -2.4 placebo)
- Statistical separation at every assessed time point

Secondary endpoint: PANSS-negative sub-scales



Clinically meaningful and statistically significant improvement in PANSS negative vs. placebo

- 2.3 point improvement at week 5 with p<0.001 (-3.2 KarXT vs. -0.9 placebo)
- Statistical separation at every assessed time point

Summary of safety and tolerability

Overall Safety & Tolerability:	**Overall discontinuation rate on KarXT (20%) similar to placebo (21%)** **The number of discontinuations due to treatment emergent adverse events was equal in the KarXT and placebo arms** (N=2 in each group) **Dose escalation rate on KarXT was high and similar to placebo** • **91% of KarXT subjects escalated to 125/30 KarXT** (vs. 97% on placebo); • **4% percent de-escalated back to 100/20 KarXT dose** (vs. 1% on placebo)
AEs Observed with KarXT:	**Overall treatment emergent adverse event rate on KarXT was 54% vs. 43% on placebo** • Most common adverse events were constipation, nausea, dry mouth, dyspepsia, and vomiting, which were all mild or moderate in severity and did not lead to discontinuations • One serious adverse event on KarXT: patient discontinued treatment and subsequently sought hospital care for worsening psychosis, meeting the regulatory definition of an SAE. All other TEAEs were mild or moderate • No syncope, no mean change in BP, 5.5 bpm peak mean placebo adjusted resting HR increase with downward trend after week 2, and one discontinuation due to elevated GGT
KarXT lacks key problematic side effects of current antipsychotics:	**The rates of the following AE were similar for KarXT and placebo:** • Somnolence • Weight gain • Extrapyramidal symptoms/akathisia
Key take-aways:	**KarXT was well tolerated with a discontinuation rate equivalent to placebo and was not associated with the most common problematic adverse events of current antipsychotic medications**

KarXT Development Plan

Multiple efficacy and safety studies support Phase 3 development of KarXT

Three double-blind, placebo-controlled studies supporting therapeutic benefit of xanomeline/ KarXT

- ✓ KarXT Phase 2 study in patients with schizophrenia
- ✓ Small Phase 2 study in patients with schizophrenia with xanomeline-alone
- ✓ Phase 2 study in elderly patients with Alzheimer's disease with xanomeline-alone

Large existing safety database with xanomeline and KarXT:

- ✓ >1000 patients enrolled in studies with KarXT or xanomeline across 20 human clinical trials
- ✓ 68 elderly Alzheimer's disease patients treated with xanomeline for at least one year
- ✓ Long term preclinical safety data with xanomeline including 2-year carcinogenicity studies

Multiple positive efficacy results, large existing safety databases underscore relatively de-risked nature of KarXT compared to typical program entering Phase 3

Phase 1b healthy elderly trial foundational for Alzheimer's disease

Trial design to assess the safety & tolerability of KarXT in healthy elderly volunteers

- Similar design to previous Phase I multiple ascending dose trial in normal healthy volunteers
- Two weeks of treatment with titration over up to 10 days
- Cohorts of 16 subjects with 3:1 randomization to KarXT or placebo
- Flexible dosing to determine maximum tolerated dose on an individual patient basis

Trial Status

Trial initiated
Q4 2019

Topline results planned
H2 2020

Phase 1b experimental pain trial

Goals

- Confirm preclinical analgesic signal in healthy volunteers using an induced-pain model
- Inform most appropriate Phase 2 pain indication (acute/inflammatory/neuropathic)

Trial Synopsis

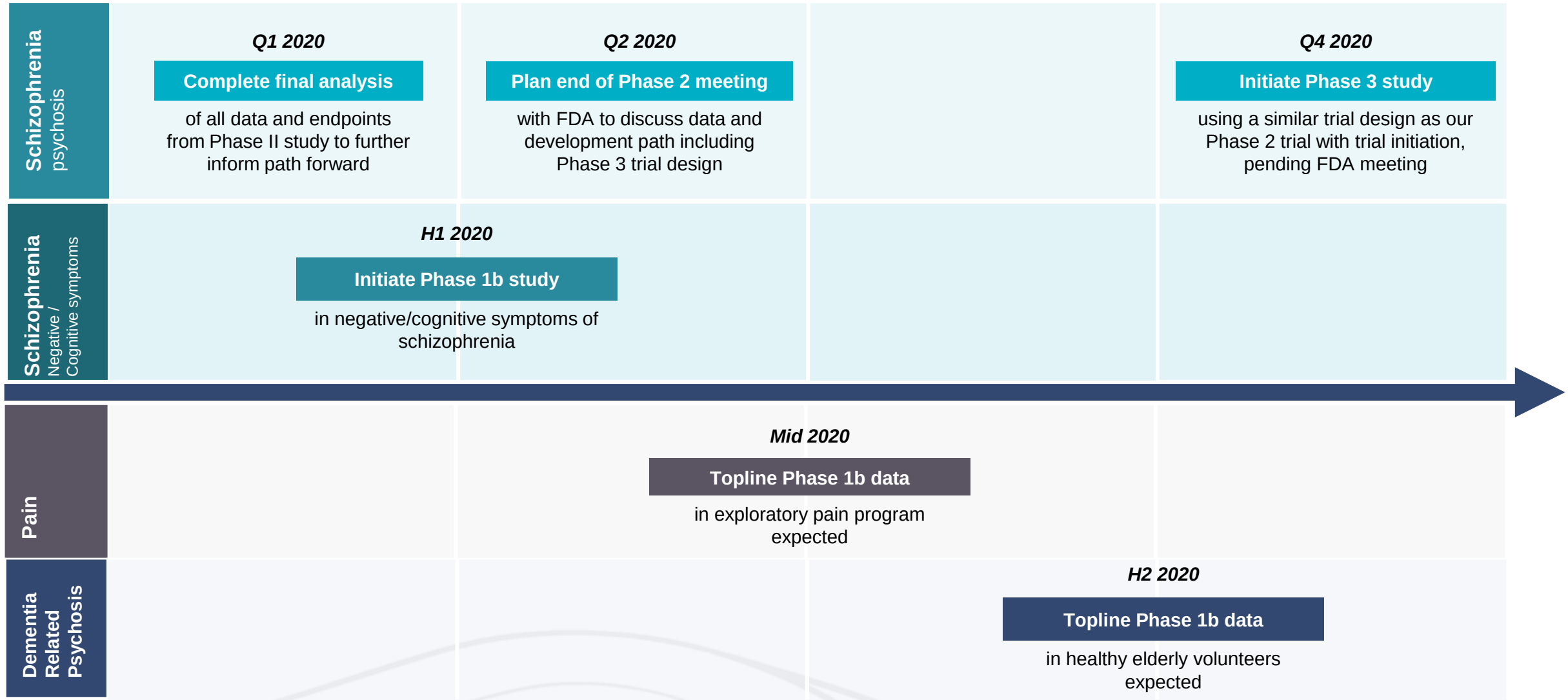
- Randomized, 4-way crossover in 24 healthy subjects
- 3 dose levels of KarXT vs. placebo
- 4 days of dosing with 2-week washout in-between
- Both subjective (standard visual analogue scale) and objective (EGG measurement of evoked potential) outcome measures

Trial Status

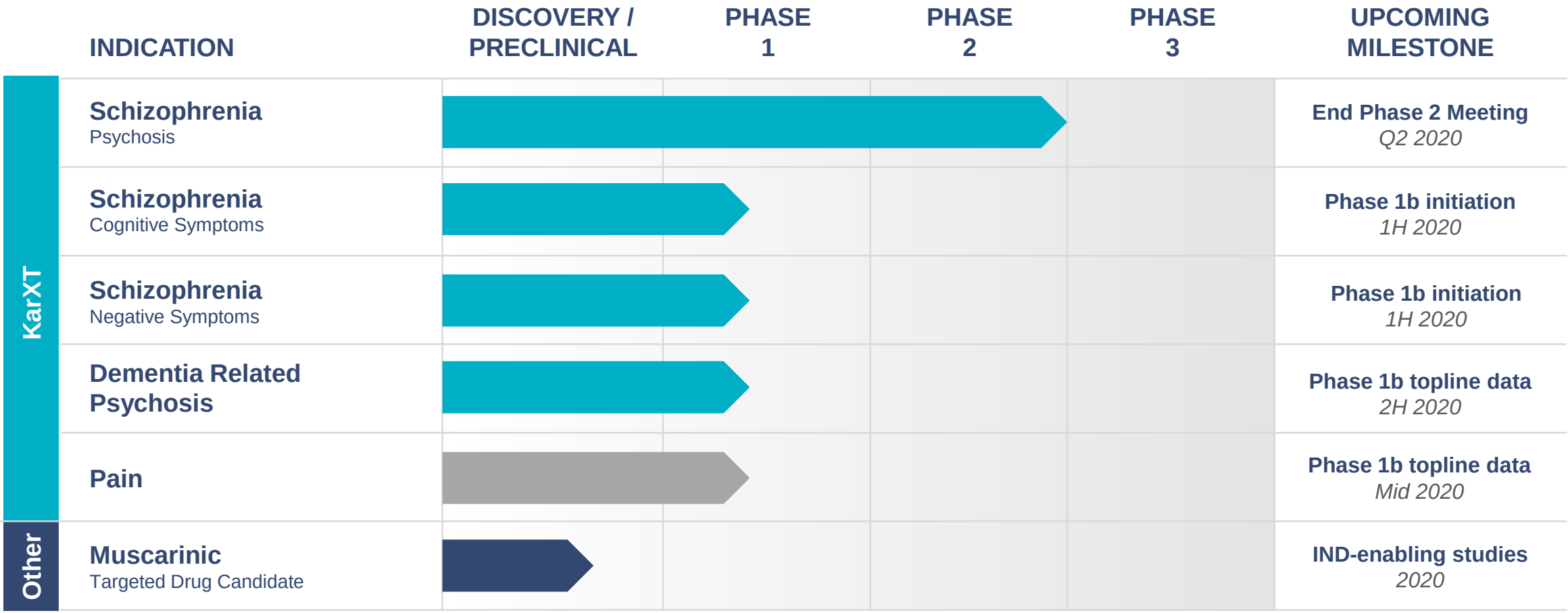
Trial initiated
Q4 2019

Topline results planned
Mid-2020

KarXT development in 2020



Karuna's portfolio of muscarinic receptor-targeted programs



Financial information at a glance

$162m
CASH ON HAND[1]
AS OF SEPTEMBER 30, 2019

$250m
RAISED IN NOVEMBER 2019
PUBLIC OFFERING

Current funding supports:

- ✓ **Filing of a New Drug Application with the U.S. Food and Drug Administration** for the treatment of psychosis in schizophrenia, including two Phase 3 clinical efficacy studies and required long term safety study
- ✓ Completion of Phase 1 and 2 trial for treatment of dementia-related psychosis
- ✓ Completion of Phase 1 and 2 trial for treatment of pain
- ✓ Continued investment into pipeline expansion

Cash expected to fund operations through at least the second half of 2021

Current Analyst Coverage

Goldman Sachs
citi
WELLS FARGO
WEDBUSH
William Blair
STIFEL
JMP

[1]*Includes cash, cash equivalents and short-term investments*

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