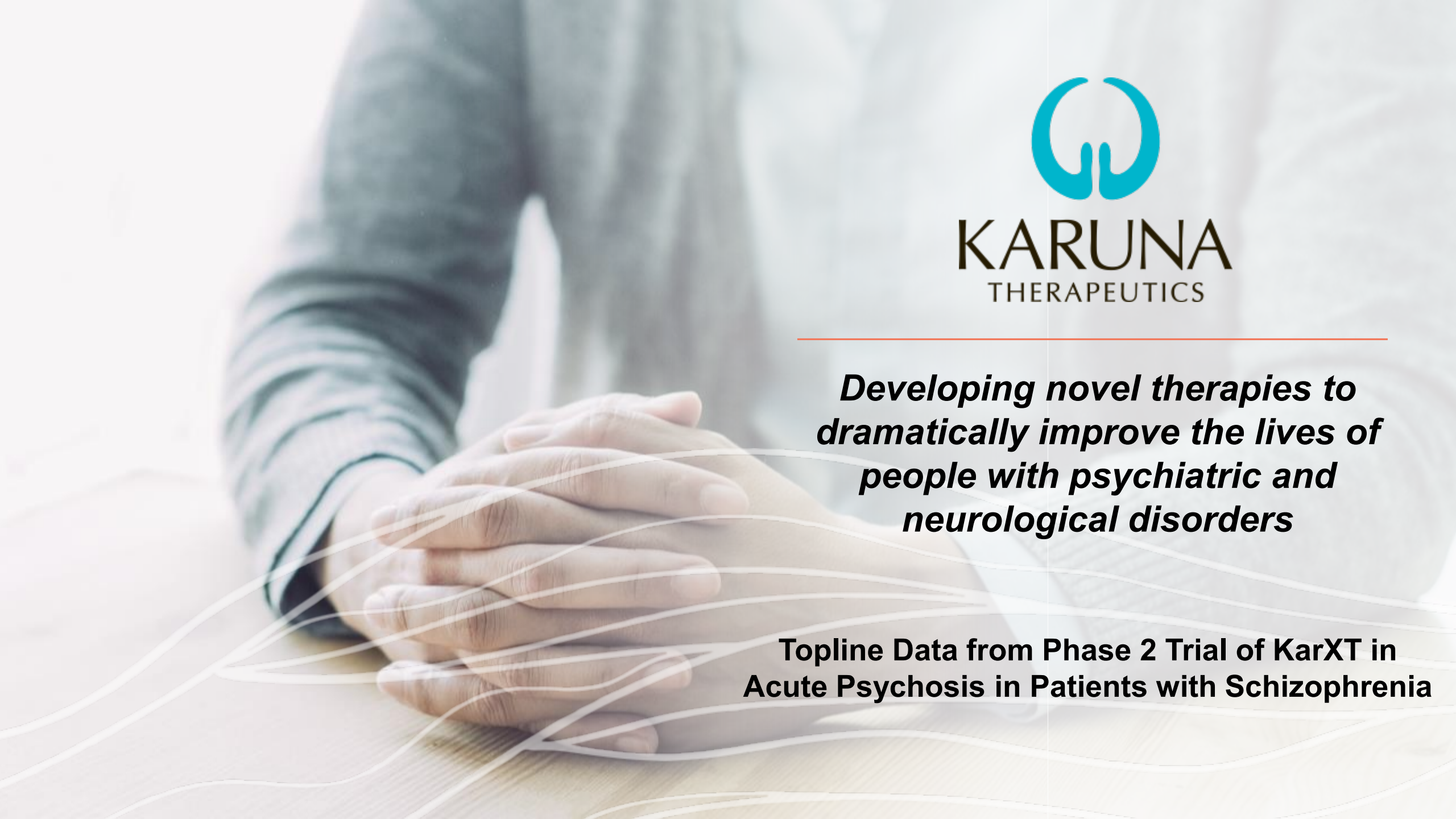

KARUNA
THERAPEUTICS

Developing novel therapies to dramatically improve the lives of people with psychiatric and neurological disorders

Topline Data from Phase 2 Trial of KarXT in Acute Psychosis in Patients with Schizophrenia

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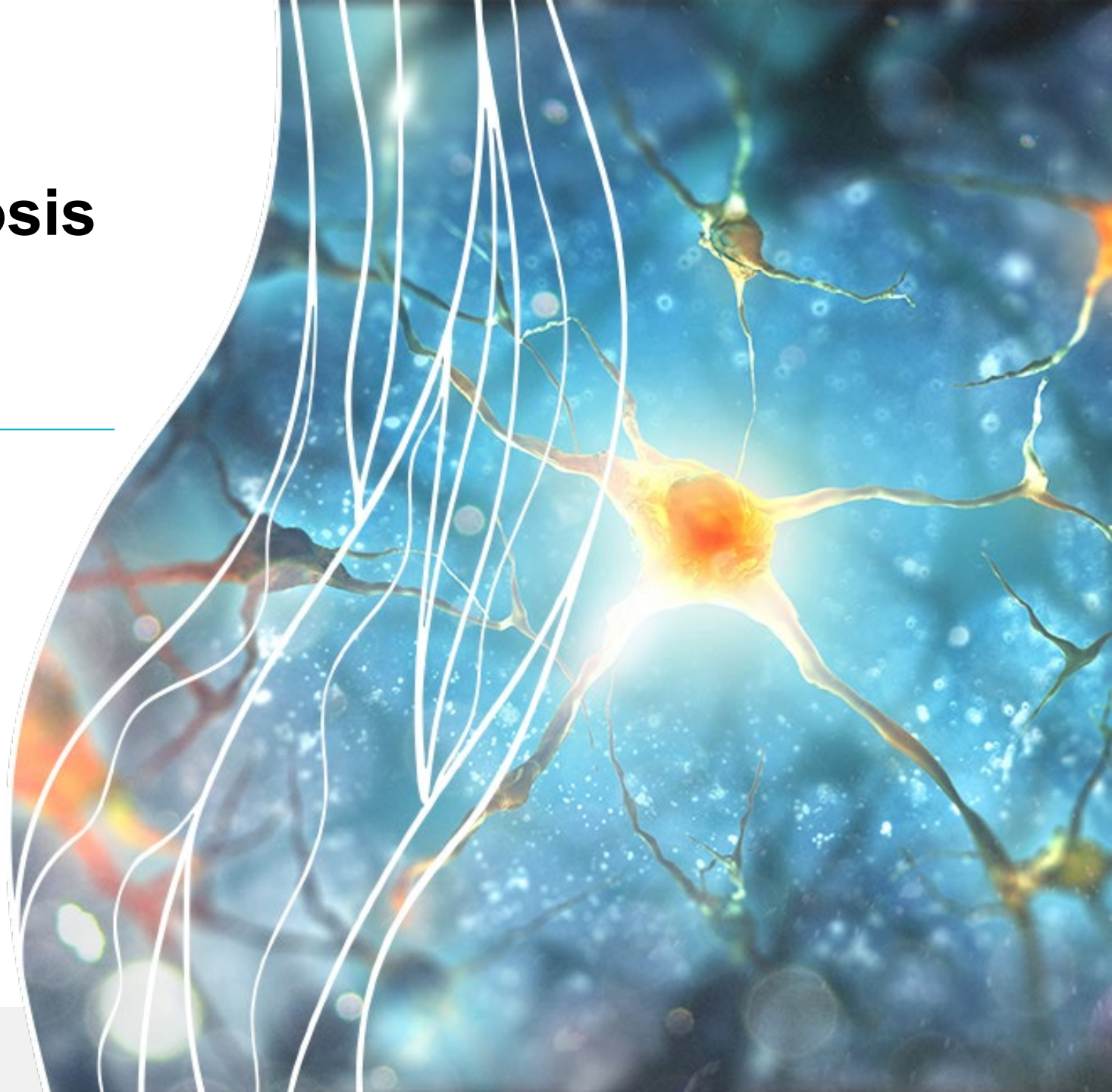
Agenda

Introduction	Troy Ignelzi / Chief Financial Officer
Summary of Phase 2 Results	Steve Paul, M.D. / Chairman, CEO and President
Phase 2 Results Analysis	Stephen Brannan, M.D. / Chief Medical Officer
KarXT Development Plan	Andrew Miller, Ph.D. / Founder & Chief Operating Officer
Summary Remarks	Steve Paul, M.D. / President & Chief Executive Officer
Questions & Answers	Steve Paul, M.D. / President & Chief Executive Officer Andrew Miller, Ph.D. / Founder & Chief Operating Officer Stephen Brannan, M.D. / Chief Medical Officer

KarXT Phase 2 Trial Results in Acute Psychosis in Patients with Schizophrenia



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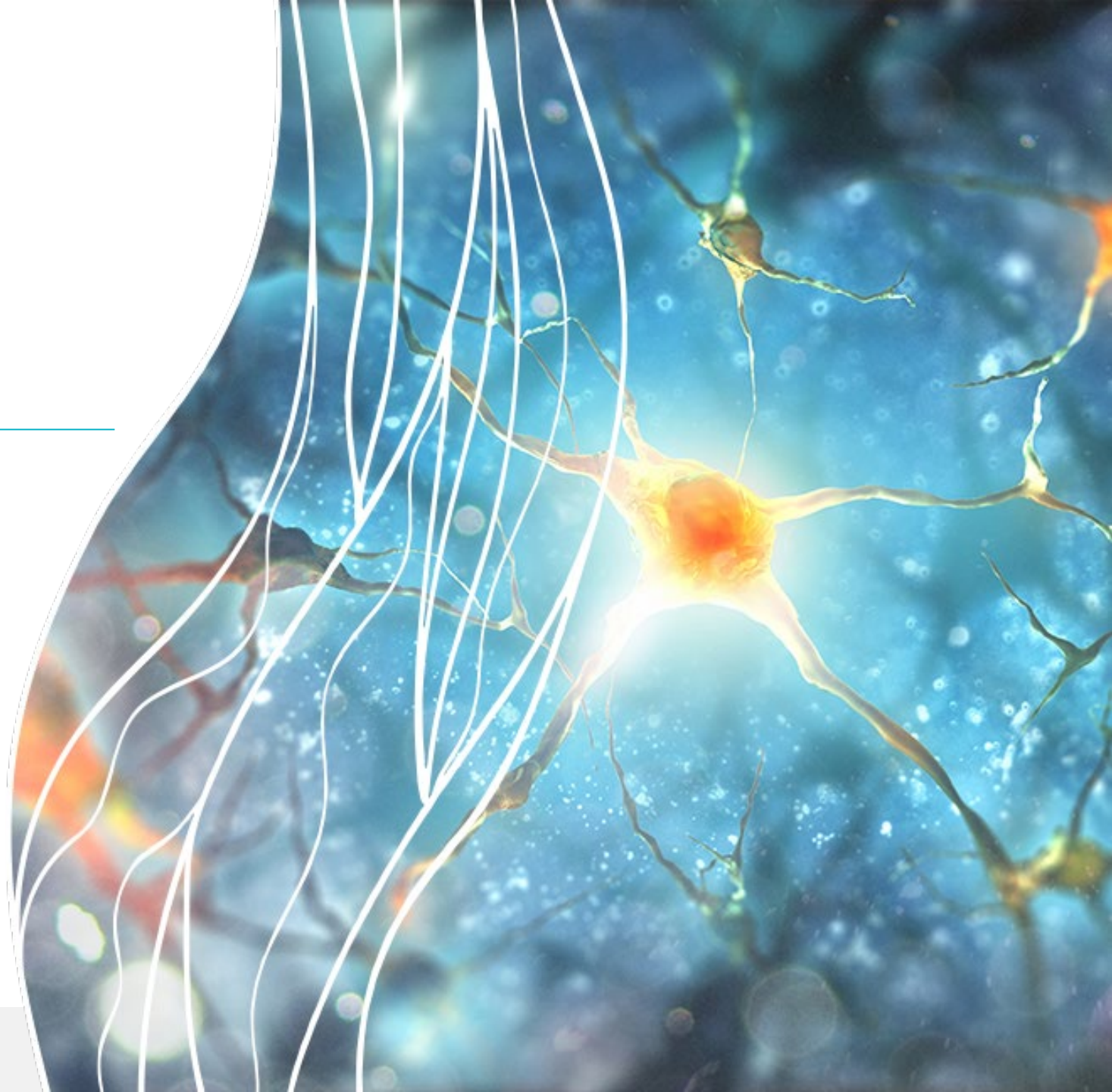
Schizophrenia: The “cancer of psychiatry”

- **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 rely **on same mechanism as drugs of the 1950s** (first antipsychotic drug, chlorpromazine, discovered in 1952)
- In many patients, approved antipsychotics offer **modest efficacy and significant side effects**

Summary of Topline Phase 2 Results

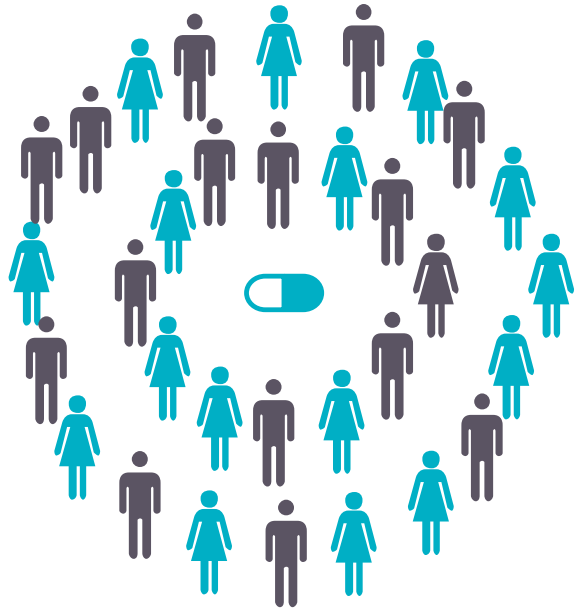
- KarXT is a novel mechanism of action therapeutic targeting central nervous system (CNS) indications representing large and underserved patient populations characterized by psychosis and cognitive impairment
- Met the primary endpoint with a statistically significant (P<0.0001) and clinically meaningful 11.6 point improvement on the PANSS total score from baseline vs. placebo. The PANSS total improvement over placebo was significant at all assessed time points.
- Statistically significant reduction in the secondary endpoints of PANSS-positive and PANSS-negative subscales at all assessed time points.
- KarXT was well tolerated:
  - The overall discontinuation rate and the discontinuation rate due to treatment emergent adverse events on KarXT was similar to placebo
  - 91% of patients escalated to the high dose of KarXT as part of the flexible dose design
  - No evidence of somnolence, extrapyramidal side effects or weight gain
- Data supports entering Phase 3 development with a completely unique new mechanism to treat psychosis in schizophrenia

KarXT Phase 2 Trial Results Analysis



Phase 2 Trial Design Overview

- Same fundamental trial design and primary endpoint used in pivotal studies to support registration of other antipsychotic drugs
- Randomized, double-blind, placebo-controlled, five week, inpatient trial
- Enrolled 182 schizophrenia patients with acute psychosis (N=90 on KarXT, N=92 on Placebo)
- Patients were washed out of any antipsychotic drugs prior to randomization
- Flexible dose, two-arm trial with 1:1 randomization to KarXT or placebo with a five-week treatment period
  - 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*
- Primary endpoint of change in total PANSS from baseline vs. placebo at week 5 in the modified intent to treat population (mITT)
- Other endpoints: PANSS-positive and –negative subscales, CGI, PANSS Marder factor, cognitive battery, and others



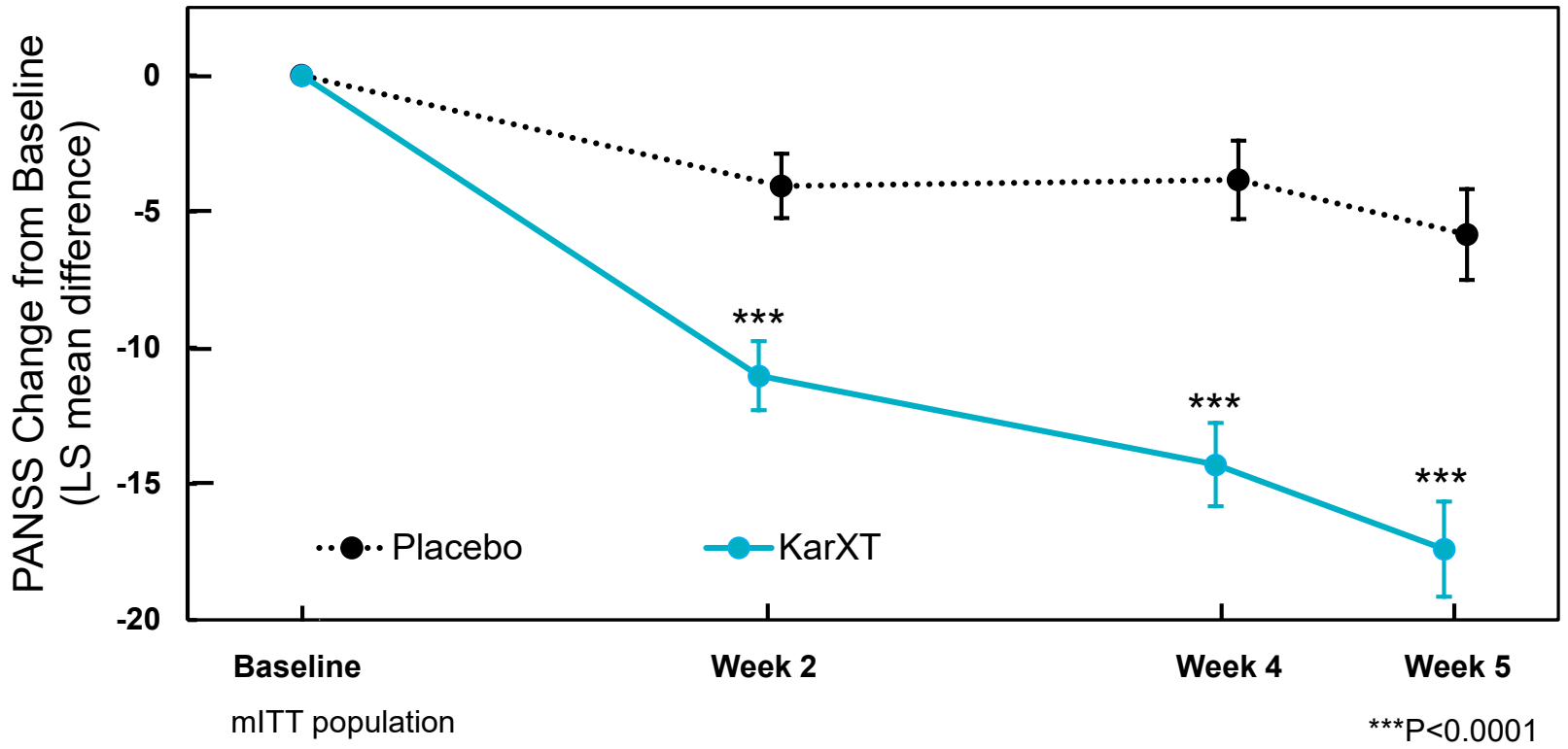
Demographics and Baseline Characteristics

	Placebo	KarXT
Mean age (years)	41.8	43.7
Sex, male (%)	74	81
Race (%white / %non-white)	20/80	23/77
Baseline PANSS	96.6	97.3
Baseline PANSS-positive	26.3	26.3
Baseline PANSS-negative	22.9	22.5

mITT population

- No significant differences between the treatment groups

Primary Endpoint: PANSS Total Score at Week 5

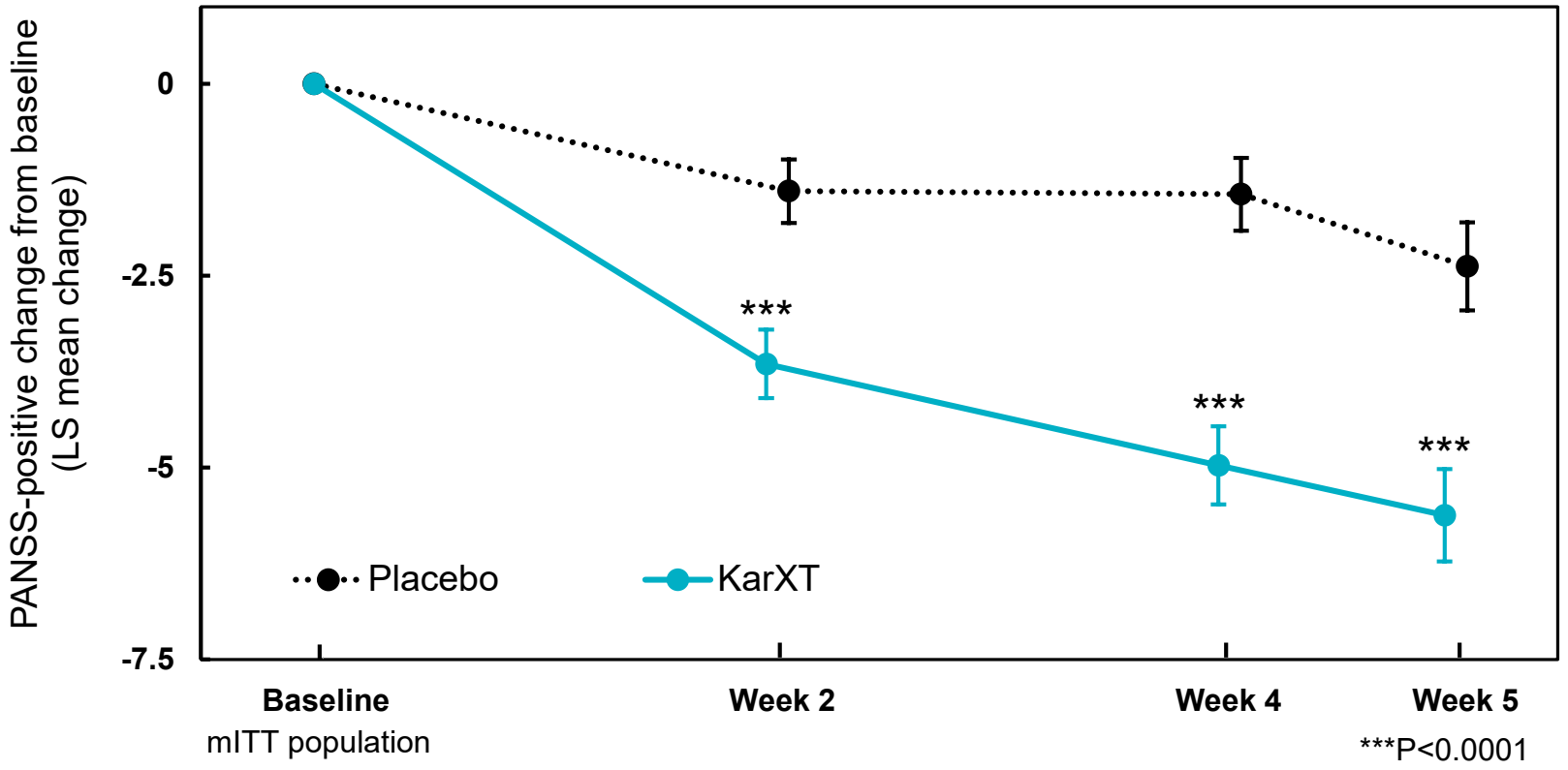


mITT population

***P<0.0001

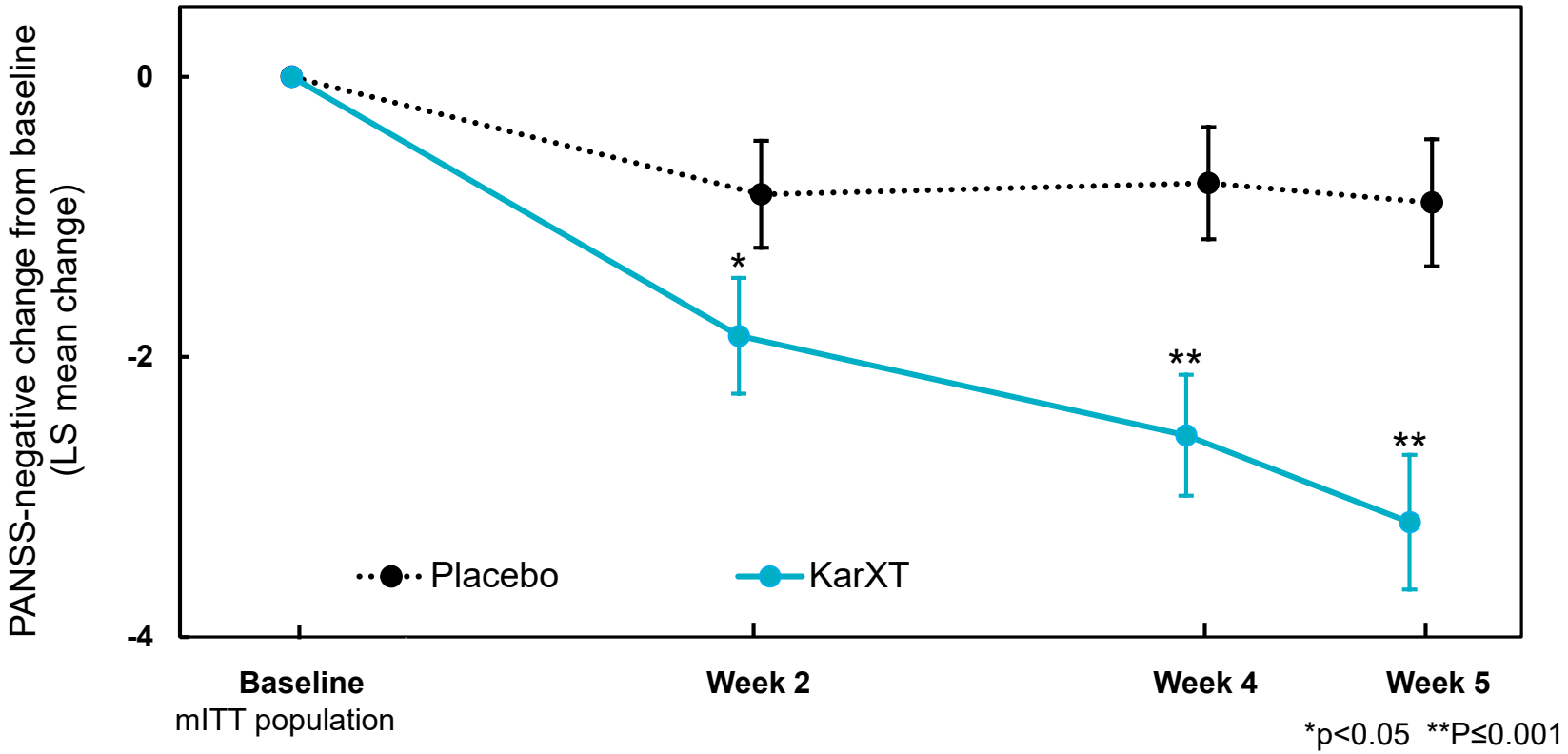
- Clinically meaningful and statistically significant improvement in total PANSS vs placebo
- 11.6 point improvement at week 5 with p<0.0001 (-17.4 KarXT vs. -5.9 placebo)
- Statistical separation at every assessed time point

Secondary Endpoint: PANSS-Positive Subscore



- Clinically meaningful and statistically significant improvement in total 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 Subscore



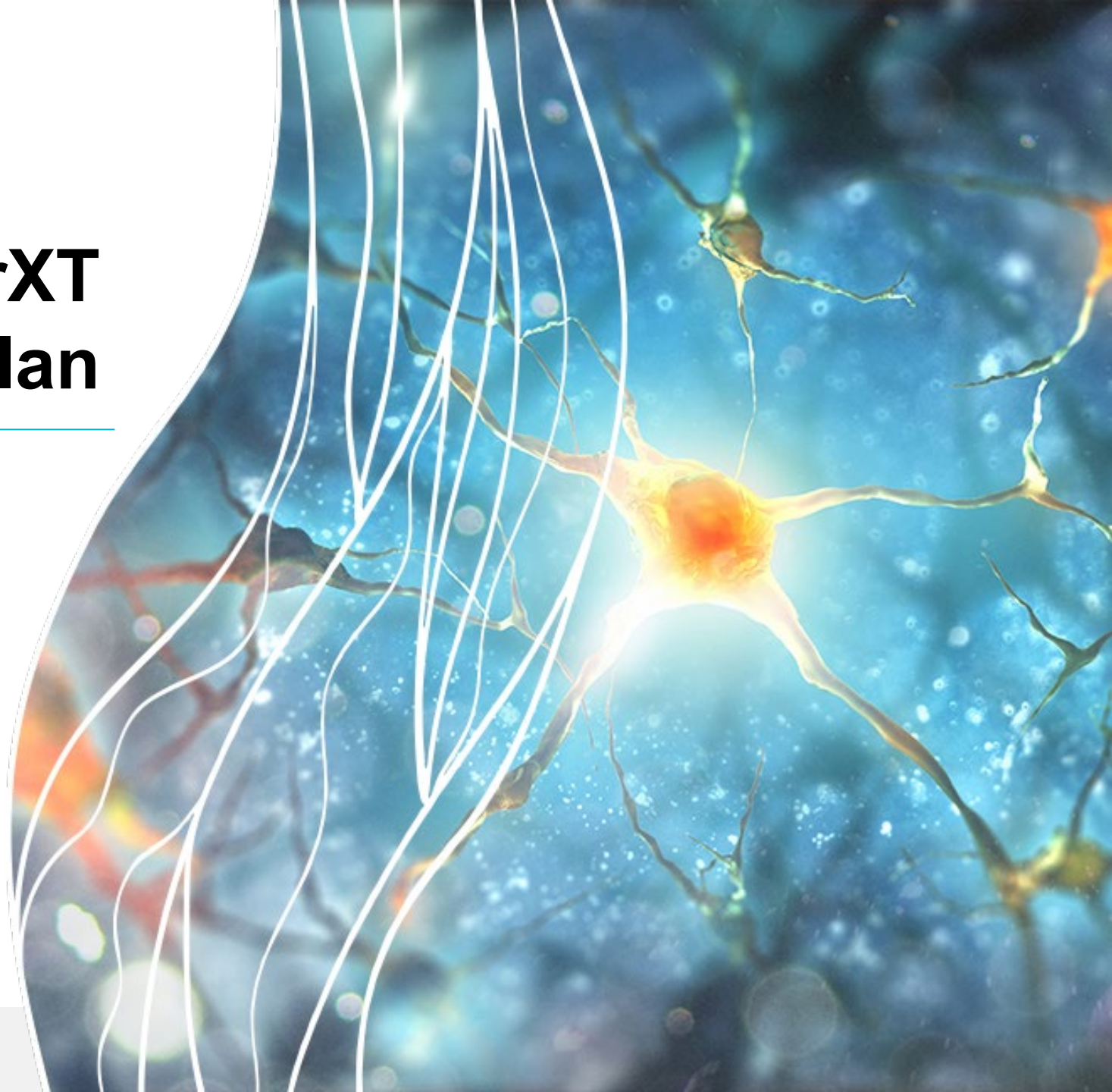
- Clinically meaningful and statistically significant improvement in PANSS-negative vs placebo
- 2.3 point improvement at week 5 with p<0.001 (-3.2 KarXT vs. -0.9 placebo)
- Statistical separation at every assessed time point

Summary of Safety and Tolerability

- KarXT was well tolerated
  - 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)
  - 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
  - Somnolence, weight gain, and extrapyramidal symptoms/akathisia similar to placebo
  - 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
  - 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

data from safety population

KarXT Development Plan



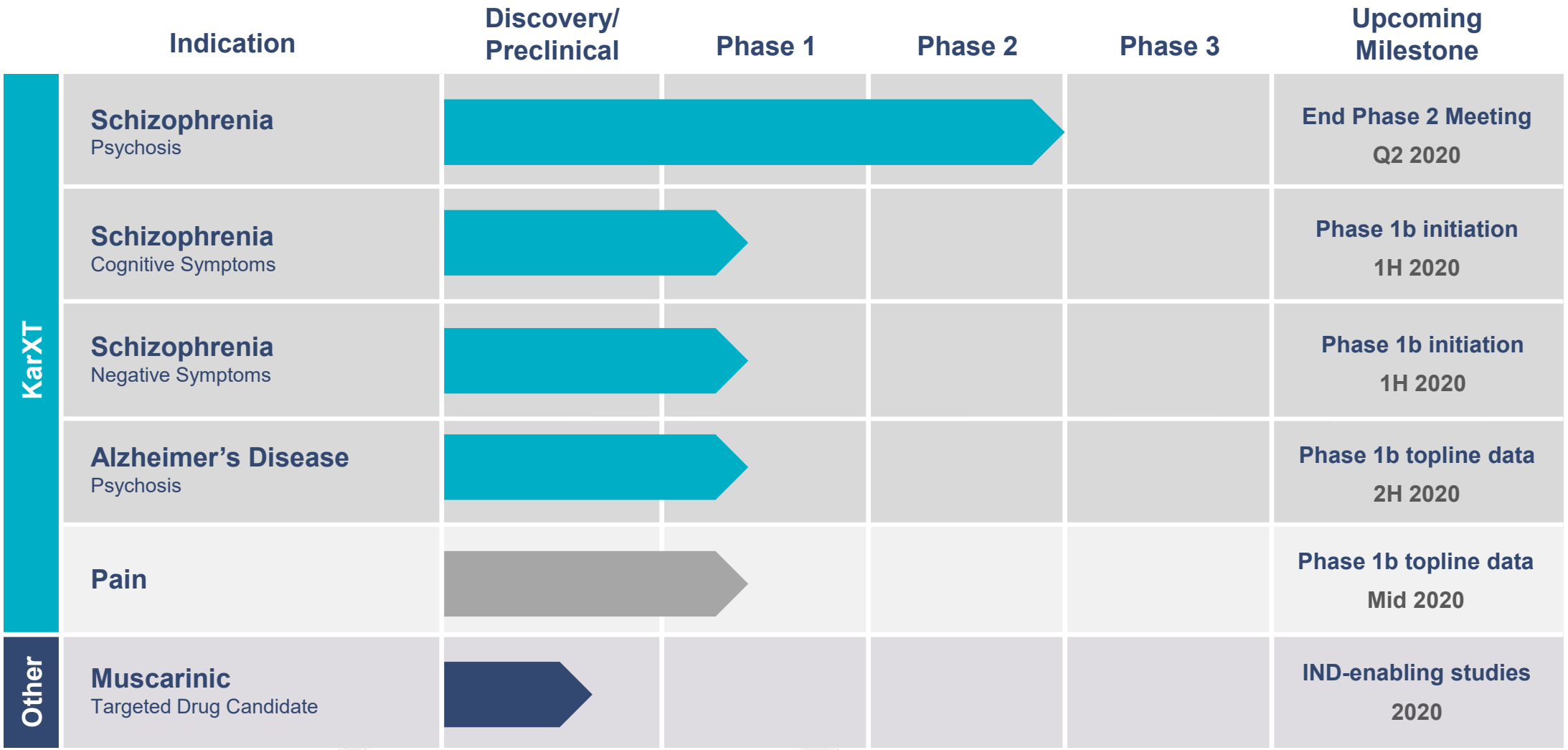
Multiple efficacy and safety studies support Phase 3 Development of KarXT

- Achieved the initial goals of KarXT development:
  - Improve tolerability of xanomeline
  - Maintain and confirm previous therapeutic benefits of xanomeline
- 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 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
  - 68 Alzheimer's disease patients treated with xanomeline for at least one year
- Robust data including 3 efficacy studies and long-term safety going into Phase 3

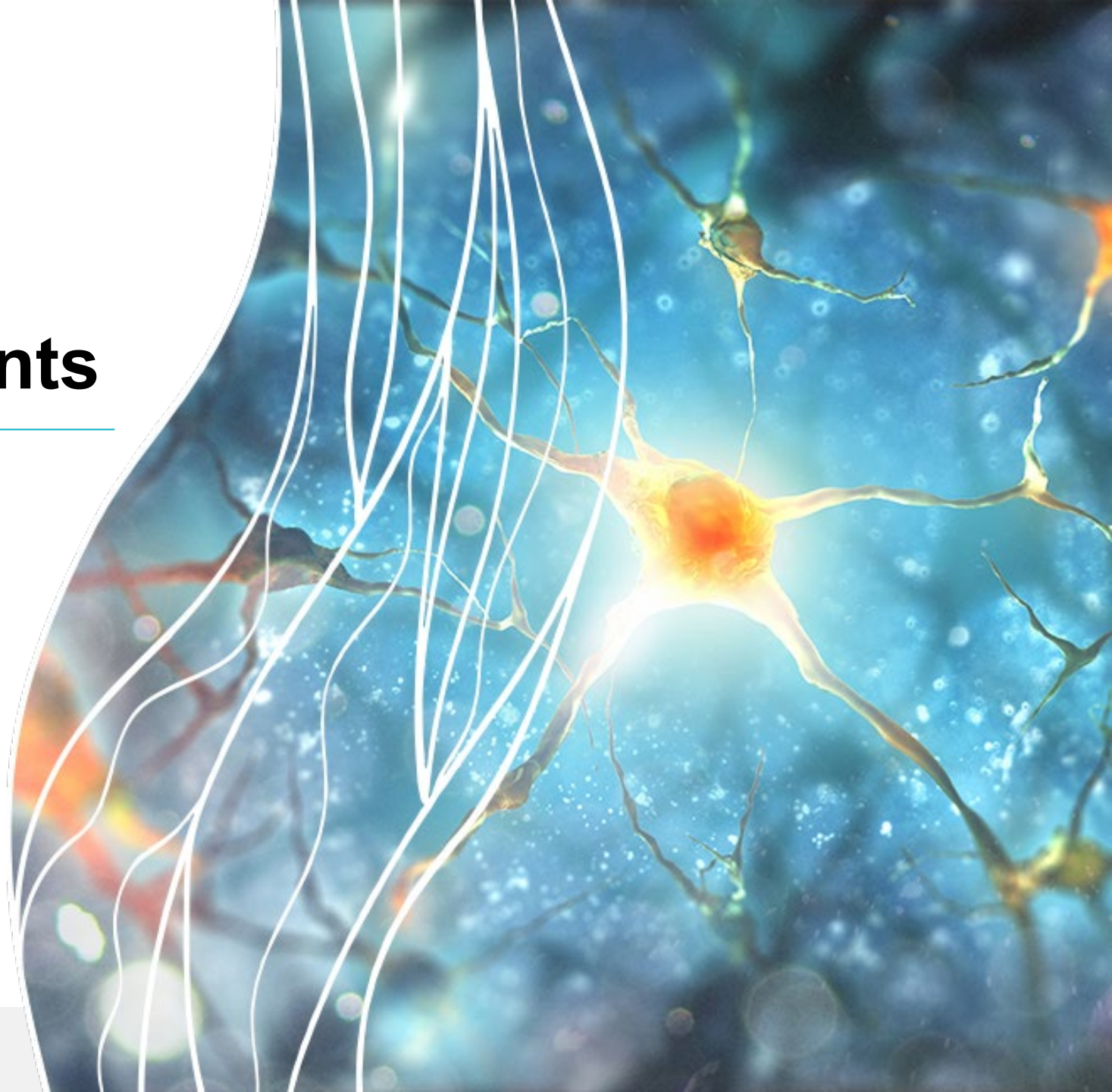
KarXT Development Moving Forward

- Complete final analysis of all data and endpoints to further inform path forward
- Plan an end of Phase 2 meeting with FDA to discuss data and development path including Phase 3 trial design
  - Meeting anticipated in Q2 2020
- Pending FDA meeting, we anticipate advancing to Phase 3 using a similar trial design as our Phase 2 trial with trial initiation anticipated by the end of 2020
- Topline Phase 1b data in pain expected in mid 2020
- Topline Phase 1b data in healthy elderly volunteers expected in 2H 2020

Karuna's portfolio of muscarinic receptor-targeted programs



Summary Comments



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