Praxis Precision Medicines, Inc.
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From genetics to precision medicines for central nervous system disorders

Praxis Precision Medicines, Inc. uses a genetics-driven approach to develop potential best-in-class drugs for patients with central nervous system (CNS) disorders that are characterized by faulty electrical activity in the brain.

Genome-wide association studies have revealed genetic variants that cause an imbalance in the excitation and inhibition of neuronal brain circuitry across a range of central nervous system (CNS) disorders, including essential tremor and epilepsies. Researchers at Praxis Precision Medicines, Inc., a clinical-stage biopharmaceutical company based in Boston, Massachusetts, are using this knowledge to rapidly develop life-transforming therapies that target the underlying causal mechanisms of both common and rare brain disorders, using genetics to increase the probability of success (Fig. 1).

The company, founded in 2015, has accelerated since emerging from stealth mode and its initial public offering in October 2020. It now employs approximately 125 people to advance its growing portfolio of CNS precision medicines for patients. Praxis' pipeline is currently focused on two key areas of unmet need: movement disorders and epilepsy.

"The combination of our focus on genetics, the expertise of our team, and how we execute, positions us at the forefront of the development of novel CNS therapies," said Marcio Souza, president and CEO of Praxis.

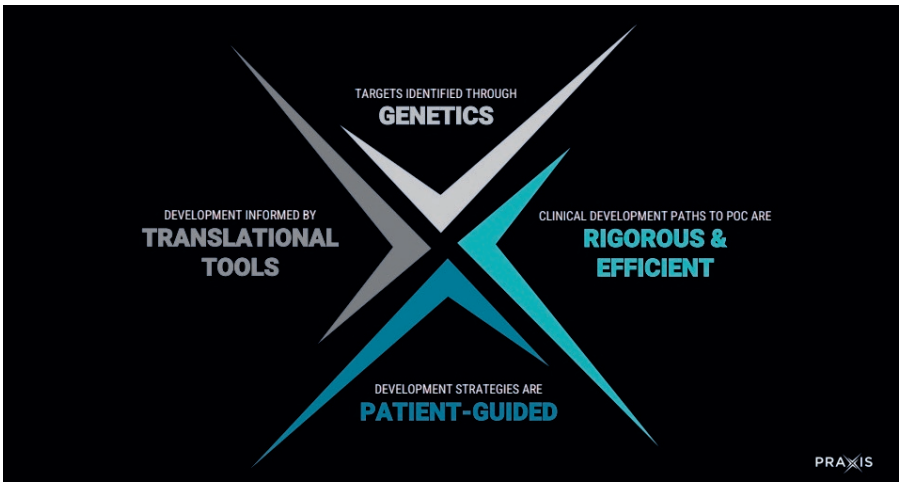

Fig. 1 | Praxis' research and development is built on four key pillars.

Transforming the treatment of movement disorders

Essential tremor is a neurological disorder that causes involuntary action tremors, most often in the upper limbs. These tremors are debilitating as they disrupt patients' ability to do normal daily activities such as eating, drinking and working, and they are often progressive.

Approximately 7 million people are affected by essential tremor in the United States, yet only one drug—the beta blocker propranolol, originally developed in 1967 to treat coronary heart disease—has been approved by the US Food and Drug Administration (FDA) for the treatment of essential tremor. Current treatment is suitable for only about 50% of patients, characterized by high discontinuation rates owing to its limited efficacy and poor tolerability, so there is significant need for a targeted treatment that restores patients' ability to function.

In May 2022, Praxis announced results from its phase 2a study with PRAX-944, a T-type calcium-channel blocker, in patients with essential tremor. The study demonstrated a marked functional improvement of 42% while patients were on treatment (measured by improvement in ability to perform activities of daily living, as recommended by the FDA), with withdrawal from treatment resulting in regression towards baseline severity. Furthermore, there was a clinically and statistically significant difference between treated and placebo patients during the randomized withdrawal phase of the study.

"We are ecstatic about the results showing clear evidence of the functional impact of PRAX-944 in essential tremor patients, finally offering hope for this community that has been underserved for decades," said Bernard Ravina, CMO at Praxis.

Praxis has already initiated its subsequent randomized, double-blind, placebo-controlled phase 2b study in essential tremor patients to evaluate the efficacy and tolerability of PRAX-944, with top-line data expected in the second half of 2022.

The company believes that PRAX-944 could also serve as a non-dopaminergic treatment for motor symptoms of Parkinson's disease, and plans to start a phase 2 proof-of-concept study in the second half of 2022.

Disease-modifying epilepsy treatments

Praxis is developing multiple therapies for both common and rare epilepsies characterized by seizures and significant developmental delay. These include a next-generation sodium current blocker, PRAX-562, which selectively dampens persistent sodium current associated with disease while aiming to spare normal neuronal activity.

PRAX-562 demonstrates robust antiseizure activity in multiple genetic epilepsy models, including SCN2A gain-of-function (GoF), SCN8A GoF, KCNQ2 and KCNC1. Furthermore, phase 1 data indicate that PRAX-562 is well tolerated, with no maximum tolerated dose identified to date at exposures well above the expected therapeutic range, and it is active in the brain, as measured by an auditory steady state response (ASSR) biomarker. A phase 2 clinical study in children with SCN2A GoF epilepsy, SCN8A GoF epilepsy, and tuberous sclerosis complex is expected to start later this year.

Praxis also has two other epilepsy programs it expects to advance into the clinic this year. PRAX-222 is an antisense oligonucleotide (ASO) that targets SCN2A GoF variants, which cause early-onset severe epilepsy. PRAX-628 is a pan-sodium channel blocker that is selective for disease-state hyperexcitability in focal epilepsy.

With another five preclinical drug candidates in development, Praxis has the largest targeted epilepsy drug portfolio in the industry.

"We are proud of our genetics-driven approach and are committed to delivering a new wave of much-needed targeted disease-modifying therapies for people living with epilepsy and other CNS disorders," said Steven Petrou, CSO and co-founder of Praxis.

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