

## EMERGING COMPANY PROFILE

# Nine Square: taking aim at organelle function in movement disorders with computation and imaging

BY KAREN TKACH TUZMAN, SENIOR EDITOR

By combining technologies from two UCSF groups, Apple Tree Partners-built Nine Square aims to develop small molecules that overcome loss of organelle function in movement disorders.

Nine Square Therapeutics Inc. made its debut last July with a \$50 million series A round. The company is using computational chemistry and physics-based modeling from the lab of serial entrepreneur Matthew Jacobson to identify small molecule candidates, and testing their effects in disease-relevant cell types using quantitative single-cell phenotyping technology from the lab of Steven Altschuler and Lani Wu.

“Our technologies are not separate, what we observe in our platform feeds back to the chemistry,” Altschuler said.

Altschuler, Wu and Jacobson are each Nine Square co-founders and professors at the University of California San Francisco; Jacobson is also a founder of Global Blood Therapeutics Inc. (NASDAQ:GBT), Cedilla Therapeutics Inc., Circle Pharma Inc. and Relay Therapeutics Inc. (NASDAQ:RLAY).

In the near term, Nine Square is focusing on the neurodegenerative movement disorders Parkinson’s disease and amyotrophic lateral sclerosis (ALS); it also plans to develop programs for non-degenerative movement disorders including essential tremor and dyskinesias.

Apple Tree venture partner and interim CEO Spiros Liras declined to disclose the company’s molecular targets, but said Nine Square’s programs aim to work around or compensate for organelle dysfunction in the endolysosomal pathway. “The genetics points to the breakdown of organelle function intracellularly,” he said.

Using Altschuler and Wu’s single-cell imaging and machine learning technologies, the company can identify which compounds are restoring organelle function and morphology in patient-derived fibroblasts and neurons.

### COMPANY PROFILE

#### NINE SQUARE THERAPEUTICS INC.

South San Francisco, Calif.

**Technology:** Computational chemistry and quantitative cell phenotyping platform for compound discovery against neurodegenerative diseases

**Origin of technology:** Founders, Nine Square

**Disease focus:** Neurology

**Clinical status:** Preclinical

**Founded:** 2020 by Matthew Jacobson, Steven Altschuler, Lani Wu, and Spiros Liras

**Academic collaborators:** University of California San Francisco

**Corporate partners:** 1859 Inc.

**Number of employees:** 4

**Funds raised:** \$50 million

**Investors:** Apple Tree Partners

**CEO:** Spiros Liras

**Patents:** Not disclosed

The machine learning analysis of compounds’ effects needs to be “human-auditable and biologically understandable,” Altschuler said. “Prediction is not sufficient, you need to understand what is the defect,” said Wu.

The company will draw on physics-based modeling techniques from Jacobson’s lab to generate small molecules capable of getting into the brain and desired intracellular compartments. “It’s reducing the amount of empirical testing it takes to thread the needle to get all these properties,” he said.

Liras said the company will likely first seek proof of concept in genetically defined subsets of its target diseases, but believes

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the benefits of correcting organelle dysfunction could carry over into idiopathic forms of the indications.

He expects the company will develop unique products for different indications, but thinks some compounds could work across a spectrum of neurodegenerative diseases.

According to Liras, the company has enough runway to last into 2024 or 2025, by which time it plans to have entered the clinic.

Another company using imaging-based phenotypic screens and machine learning to identify candidates for neurological diseases is Recursion

Pharmaceuticals Inc. (NASDAQ:RXRX), which raised \$436.4 million in an upsized April IPO that valued the Utah-based company at nearly \$3 billion. The company has programs in Phase I testing for cerebral cavernous malformation, GM2 gangliosidosis, neurofibromatosis type 2, and familial adenomatous polyposis.

Nine Square's focus on genetic drivers of neurodegeneration is part of a larger trend that has seen early stage investors increasingly fund new ventures in the space.

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