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Neuropsychiatric Drug Developers Show a Renewed Sense of Purpose

Therapeutics for depression, schizophrenia, and other neuropsychiatric disorders are targeting inflammation, stimulating neurogenesis, and taking cues from biomarkers

By **Catherine Shaffer** November 1, 2021

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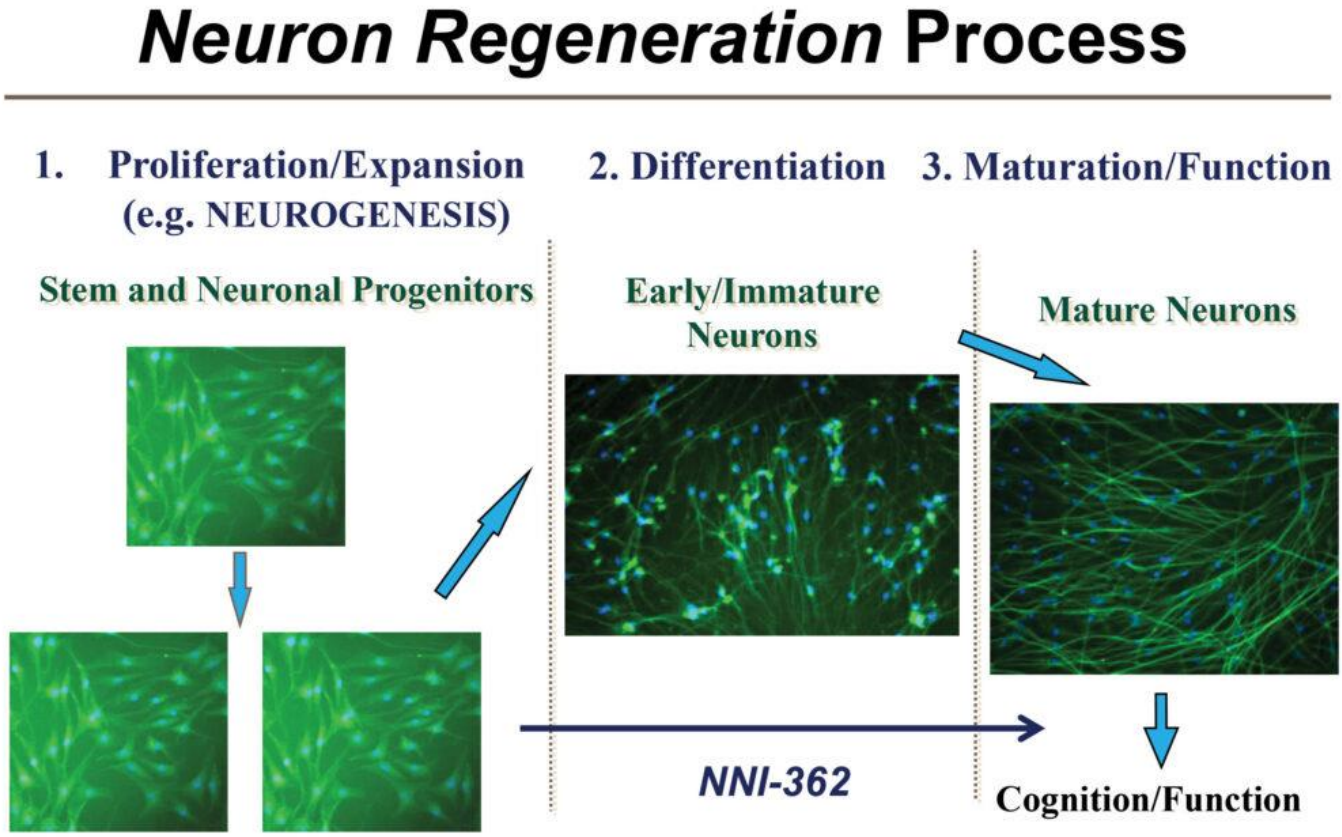
Psychiatric disorders already imposed a heavy burden on society before the COVID-19 pandemic. But now that we are dealing with COVID-19-related stress and the direct neuropsychiatric effects of the SARS-CoV-2 virus, the burden is beginning to feel all but crushing. We would welcome therapeutic relief, but so little is available. Why should so few drugs be available in this time of crisis? Until recently, neuropsychiatric drug development looked unpromising. Many pharmaceutical companies had stepped back from developing drugs for historically intransigent indications such as major depressive disorder, Alzheimer's disease, and schizophrenia. However, advances in areas such as genomics and imaging, as well as breakthrough discoveries in the pathophysiology of neuropsychiatric diseases, have prompted a new round of innovation. What follows is a look at five companies—some large, others small—that are moving forward with novel therapeutics for patients who not only have unmet needs, but who also tend to be overlooked or marginalized in society. These companies delivered some of the most compelling presentations at the Fourth Annual Neuropsychiatric Drug Development Summit, a virtual event that was held September 28–30, 2021….

Stimulating Neurogenesis

In an effort to search outside of the range of targets that have been previously tested in major neuroscience indications, NeuroNascent is studying compounds that promote neurogenesis in the brain, a natural process active throughout the lifespan of the human brain. To find those compounds, the company carried out phenotypic screens using human neural progenitor cells. Then, the company determined which of the neurogenesis-promoting agents were also neuroprotective. This process turned up hits for multiple

families of small-molecule compounds, including NeuroNascent's lead candidate for Alzheimer's and Parkinson's diseases, NNI-362.



NeuroNascent discovers and develops therapies that treat central nervous system disorders by replacing and enhancing neuron numbers, not just neural connections. One of the company's small-molecule regenerative candidates is NNI-362. Evidence that NNI-362 promotes neuron regeneration from proliferation and expansion through differentiation and maturation supports the drug's use to halt and reverse Alzheimer's disease and other age-related neurodegenerative disorders.

Judy Kelleher-Andersson, PhD, president and CEO of NeuroNascent, explains, "Using a phenotypic screen, you're allowing the modification of a cellular function to dictate the therapeutic as well as the target." Although phenotypic screening is not exclusive to the neuroscience field, it is becoming popular as an alternative to target-based screening for neurodegenerative diseases because it does not require specific knowledge of the targets or pathways involved in the etiology of these diseases. Phenotypic screens can also point back to new, previously unknown pathways or mechanisms. Meanwhile, target-based drug discovery has repeatedly failed to produce disease-modifying therapies, even as the industry continues to carry the torch for targets like β-amyloid. NeuroNascent has completed a Phase Ia trial of NNI-362 in a healthy, aged population and found that the drug was safe and well tolerated. The next step, once funding is secured, will be a proof-of-concept, Phase II trial in Alzheimer's or Parkinson's patients. Keller-Andersson says that NeuroNascent scientists were able to observe neuronal regeneration in rodents that

had received about six weeks of treatment. She adds that in aged humans, the corresponding treatment time would probably be six to nine months. Treated patients would be evaluated with volumetric magnetic resonance imaging to assess whether new neurons had been integrated in the brain. Also, treated patients would be assessed for reversals in age-related deficits. The company is also developing a compound called NNI-351. NNI-351 is undergoing IND-enabling testing for the treatment of rare pediatric disorder fragile X syndrome. Kelleher-Andersson says that this compound has reversed the hippocampal-related behavioral deficits in an animal model of fragile X syndrome.