



7th Annual

Neuropsychiatric Drug Development Summit

Fuelling Next Generation Neuropsychiatric Approvals

Exclusive Interview With:



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How has the psychiatry treatment landscape evolved over the last 12 months and where do you see it heading in the next few years?

Our focus in the Stanley Center at Broad is on schizophrenia and bipolar disorder, and so the last 12 months have been particularly exciting largely because of the positive results around muscarinic receptor agonism (e.g. KarXT), which appears poised to become the first novel mechanism of action for schizophrenia treatment since the original antipsychotics were serendipitously discovered almost 70 years ago. It's hard to overstate how exciting it would be to finally have a new class of drug for schizophrenia, not only for the impact on patients but also for the motivation and interest it generates with researchers and companies to see that success is possible in this space. My hope is that this is only the beginning, and that the interest industry is now showing in psychiatry in general, and schizophrenia in particular, is not just the start of another boom-and-bust cycle but the foundation of a sustained investment.

Following recent approvals, with more anticipated this year, where is the field looking next to develop more effective, differentiated and transformative therapies for mental health disorders?

Again, treatment options for serious mental illnesses have been stagnant for decades; essentially any progress in psychosis or major depression would almost by definition be differentiated and transformative. From an academic researcher's perspective, the muscarinic agonists are very exciting but once again serendipitous—these drugs were initially developed for cognitive impairment in Alzheimer's, and just turned out to have antipsychotic effects. On the other hand, the past ten years have seen incredible progress in the genetics of schizophrenia, bipolar disorder, and major depression, and the follow-up neurobiology, for example around neuroimmune signalling and synaptic dysfunction, is beginning to emerge. The success of KarXT should not keep us from pursuing new therapeutic hypotheses that are based on the specific biology of these disorders.

What would you say are the most promising new targets in development to tackle specific mood or behavioural symptoms?

Again, it is wonderful to have a new class of antipsychotic, but there are still no drugs that specifically address the negative, affective or cognitive symptoms of schizophrenia. I'm excited about trials underway for KarXT as well as other targets like GlyT1 that are specifically designed to

assess cognitive improvements. I'm not as familiar with all the specific targets in development across industry, but I think cognition is the symptom domain I'm most interested in seeing tackled in the near future, as we learn more about how genetic risk factors for serious mental illnesses impact synapse and circuit functions. I also think there's a huge amount of space to be explored in combining small molecules with cognitive and behavioural interventions. We often talk about schizophrenia for instance as being a circuit-based disease, and therefore about the difficulty of treating specific circuits by targeting proteins that are widely distributed throughout the brain. The idea of combining a synapse-targeting drug with a behavioural intervention that activates the most relevant circuits seems like a great direction for both preclinical and clinical research.

Which specific challenges are you looking forward to addressing with colleagues at the Neuropsychiatric Drug Development Summit in order to collaboratively propel advancements?

Coming from the academic research side, I'm very excited to talk to industry colleagues about how we can collaborate to translate basic biology insights into molecular biomarkers that would enable the identification of transdiagnostic subgroups that can be matched to the right trials and the right treatments. This seems like a huge unmet need but also a fruitful space for pre-competitive collaboration, as it will take significant investment and require both academic and industry expertise.

Which sessions in the agenda are you most looking forward to at the 7th Neuropsychiatric Drug Development Summit?

There look to be some great sessions throughout but as you might guess from some of my previous answers, I'm excited for some of the discussions in the Day 1 discovery and preclinical track around novel targets and circuits as targets. Should be great!

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