In neuroscience, “an inflection point in knowledge and technology”

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Bob Baloh’s interest in drug development’s potential was piqued early in graduate school. At the time, he was working in a lab making growth factors that had potential applications as therapeutics for patients with Parkinson’s disease.

“That’s where I first saw how you could use science to make medicines, and I thought that was the coolest thing ever,” he says.

When it came time to launch his career, Baloh, who is now the Head of Neuroscience at the Novartis Institutes for BioMedical Research (NIBR), opted to be a physician-scientist, a path that allowed him to help patients in the clinic while still conducting research in the lab. That research, he hoped, might one day lead to new therapeutic options for patients in his specialty of neurology, where he focused on neuromuscular diseases — particularly debilitating, genetically driven conditions such as amyotrophic lateral sclerosis (ALS), inherited neuropathies and muscular dystrophies.

In 2012, he took on his first leadership role in academic medicine, returning to his native city of Los Angeles to join Cedars-Sinai Medical Center, a world-renowned hospital system affiliated with the University of California, Los Angeles (UCLA). There Baloh was tasked with building a neuromuscular division in a growing academic neurology program.

During his tenure, he built out a large clinical trials unit for neuromuscular diseases and ran one of the largest ALS clinics on the west coast. But as much as he valued caring for patients, he knew they faced a harsh reality: there were no therapeutic options for their condition — nothing that could change the course of their disease in any meaningful way. It was a situation Baloh had encountered all too often working in the neurodegenerative disease space, and it motivated him to make the jump to industry.

In December 2021, Baloh came to NIBR. He explained his motivations for the move, his approach to strategy and leadership, and his take on the state of the field in a recent interview:

It sounds like you had a longstanding interest in drug development throughout your career. What finally persuaded you to pursue a career developing therapeutics?

After nine years building a clinical division and basic research center at Cedars-Sinai, I was being considered for a variety of leadership positions and was trying to decide what to do in the next phase of my career. One thing I recognized was that, while I was happy and proud of what I’d accomplished in leadership roles in academic medicine, as my career advanced I was not really moving toward the goal I had always wanted to pursue since graduate school: using science to make medicines. And I guess the way I would describe it is, I thought about what gets me excited to get up in the morning, and that’s making medicines and really many of the other commitments I had were distracting me from that. And I felt that, for the patient population that I was working with — ALS, Alzheimer’s, Parkinson’s, etc. — the biggest impact I could make for them would be working in early-stage drug discovery.

I think another factor was seeing the amazing progress of drug development for spinal muscular atrophy (SMA) — not just in one but three different therapeutic modalities. It said to me that we were at an inflection point in knowledge and technology, and if I was interested in concentrating all of my efforts on making therapeutics, this would be a good time.

What ultimately convinced you to come to Novartis?

Honestly, I'd have to say it was the culture and style of leadership, which I find inspiring and consistent with the way I aspire to lead. At NIBR there's an emphasis on true excellence in science and digging down to the fundamentals of how the medicines we are making actually work at the molecular and cellular level. There's also a sincere interest in developing those medicines in a way that treats the right patients at the right time.

And then on the culture side, the commitment to a curious, "unbossed" culture resonated deeply with me because I always tried to operate that way on a smaller scale with my labs and academic centers. It's important to encourage contributions from all of our people because so many have great ideas and unique experiences that they bring to the problems we're trying to solve. We're trying to do this together, so it's critical to build strong teams and leverage each other's expertise.

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> **- Bob Baloh**

How would you describe the approach that Novartis takes in neuroscience?

When I describe the three pillars of our efforts in neuroscience, I look at it chronologically. First, how does the brain develop? What are the diseases or disorders that come from abnormal development in the early stages of life? That's the science behind our neurodevelopmental portfolio, where a wealth of new genetic insights and therapeutic approaches are becoming available. Then, how does the brain function during adulthood after development? And that's the foundation of our projects in neuropsychiatry, understanding genetic drivers and brain circuitry underlying psychiatric conditions. Finally, how does the brain resist injury and age healthfully over the course of one's lifespan? That's the foundation of our neurodegeneration and neuroinflammation efforts, which are two tightly linked processes where again there are a wealth of emerging targets and biomarkers. In a nutshell, that's what we're working on in neuroscience.

Neuropsychiatry is one of the most challenging areas for drug development. Baloh suggests that more work on biomarkers, genetic stratification, and novel methodologies such as multimodal AI-driven patient stratification may be needed to make sure drugs are targeted to the right patients. Video courtesy of kerenby, via Storyblocks.

How are you going about building a strategy for this portfolio as a new leader?

When I came in, my first goal was to learn where the strategy has been, where we are right now, and then figure out where we should be going. I'd compare it to walking in and joining a chess match that's already been played for many years. You need to study the board and adapt to where you're at. What pieces do you have and where are they at this point in the match? What are your strengths and who are your collaborators? There are many different directions one could go in each of our priority areas. We could even launch new programs, new groups, new pillars of course. But none of those decisions should be made without knowing the organization, the history of the portfolio, and the people really well.

What do you see as a challenge as you move forward in drug development in neuroscience?

Neuroscience is without doubt one of the most challenging areas in drug development so I can think of a many, but one that comes to mind is neuropsychiatry. It's an area where there are established targets and of course effective drugs on the market, but there is still an unmet need and opportunity to make better medicines that reach the right patients. That means that in addition to finding new targets, we really have to think about new ways to optimize our clinical development strategies. We need better ways to better understand the patients, and whether there are biomarkers or signatures of abnormal brain function that might tell us which patients might benefit from a given therapy. Psychiatry is of course not unique in that way, but patient substratification is particularly challenging in that field. It may mean investing more in biomarkers, genetic stratification, and novel methodologies, such as multimodal AI-driven patient stratification — whatever it takes to improve our chances of getting the right drugs to the right patients.

Is there an area of research that's particularly exciting to you right now?

Across the different forms of neurodegeneration — whether it be Parkinson's Disease or progressive Multiple Sclerosis (MS) — we're placing a strong emphasis on understanding neuroinflammation. That's one of the themes I was working on in my laboratory for the last nine years, so I'm possibly biased, but I'm very excited about our opportunities to manipulate neuroinflammation, particularly microglial states, for therapeutic benefit. We generally focus on a bipartite approach. First, targeting genetically defined core drivers — the proteins or pathway known to be causally linked at least in rare forms of disease. The second part is to complement that by altering the inflammatory tissue response, because we know that neuroinflammation is important in all of these conditions and contributes to neuronal injury and disease. We're fortunate at NIBR to have a close collaboration with the Autoimmunity, Transplantation, and Inflammatory (ATI) Disease Area research group — and I don't know that there's anybody else in the industry with a better neuroinflammatory portfolio because of that deep expertise. With the multidisciplinary teams built here between neuroscience and ATI, not to mention the rest of the drug discovery experts across NIBR, I'm excited to see what we can accomplish with this combined neuroinflammatory/core driver approach.

In a Q&A, meet NIBR's Head of Neuroscience, Bob Baloh

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