

Nocion Therapeutics launches to selectively silence pain and itch neurons

- Raised \$27M Series A led by F-Prime Capital Partners and Canaan, with participation from Partners Innovation Fund, and BioInnovation Capital
- Platform company targeting neurons mediating cough, itch, pain and inflammation without the addictive properties of opioids
- Designing clinically differentiated treatments by targeting the distinct biological profile of activated sensory neurons

April 17, 2019 / Cambridge, MA – Today, Nocion Therapeutics announced plans to develop novel pharmaceuticals that will provide targeted, robust and sustained relief for the treatment of serious medical conditions including cough, itch, pain and inflammation. These pharmaceuticals are highly selective, locally confined, and silence sensory neurons activated by noxious stimuli, without inhibiting neurons mediating movement or touch. The approach is based on Nocion Therapeutics' unique understanding of how sensory neurons respond to noxious stimuli. The company's mission is to alleviate suffering for the millions of people with conditions arising from the activation of these neurons.

"Our novel approach to selectively inhibiting neurons, resulting from a fundamental understanding of how the body responds to insult, will result in differentiated therapeutics addressing a host of unmet medical needs," said Dr. Richard Batycky, CEO. "A confluence of world-class founders and venture partners positions Nocion on the right path to have a meaningful impact on patients' lives."

Addressing activated sensory neurons at the molecular level

Academic research led by two of Nocion's scientific founders, Bruce Bean, PhD, and Clifford Woolf, MB, BCh, PhD, identified a novel class of sodium channel inhibitors that inhibits signaling in activated pain or itch neurons but spares all other neurons. The researchers, based at Harvard University and Boston Children's Hospital, discovered sodium channel inhibitors modified to be positively charged that could enter neurons by passing through large-pore channels – including TRP and P2X channels – that are up-regulated and activated in inflamed nociceptors.

With support from Harvard's Blavatnik Biomedical Accelerator and Boston Children's Hospital's Technology Development Fund, the collaborating labs demonstrated that this approach can selectively inhibit active sensory neurons that are responding to external insult. The charged sodium channel inhibitors, known as nocions, are designed to only enter activated nociceptors through large-pore channels that exclusively open in response to pain and inflammation. Once inside, nocions block all sodium channels and electrical activity of the neurons. Unlike current standards of care, nocions do not cause general numbness nor loss of motor function seen with

conventional local anesthetics. Finally, due to their chemical nature, nocions can generate a robust effect that has not yet been observed by selective block of either Nav 1.7 sodium channels or specific large-pore channels. This is because nocions can target activated sensory neurons using any large-pore channel as a doorway in and block all sodium channels in these cells.

"We can use the large-pore channels opened by painful stimuli or inflammatory mediators as Trojan horses to deliver drug molecules into the cells and stop their electrical activity," said Dr. Bean. "The large-pore channels instigate the firing of the cells, but they can also be used to quench it."

Nocion's scientific founders are Dr. Bruce Bean, who is the Robert Winthrop Professor of Neurobiology at Harvard Medical School (HMS); Dr. Clifford Woolf, a Professor of Neurobiology and of Neurology and Director of the F.M. Kirby Neurobiology Center and Neurobiology Program at Boston Children's Hospital and HMS; and Dr. Bruce Levy, MD, Chief of the Division of Pulmonary and Critical Care Medicine at Brigham and Women's Hospital, Medical Director of the Brigham Lung Center, and the Parker B. Francis Professor of Medicine at HMS.

Activated sensory neurons underlie numerous conditions

Globally, cough, itch, pain and inflammation drive tens of millions of patients to the doctor every year. For cough alone, approximately 30 million Americans per year seek care in the outpatient setting.

To advance respiratory indications, Dr. Woolf and Dr. Bean joined forces with Dr. Levy, with support from Boston Biomedical Innovation Center, to show that the team's approach worked in *in vivo* models of lung inflammation and cough.

"People may not realize that cough is the presentation of itch in the lung. Medications that could work for itch and pain, such as sodium channel inhibitors, have a history of being used in pulmonary indications in clinical practice, including in my own. The unique molecular approach to selectively silence activated nociceptors, developed by my co-founders, addresses many of the limitations of traditional therapeutics in the class that prevent broader utilization, and may prove to offer better effects for patients," said Dr. Levy. "We're hopeful that these innovations may be applicable in many tissues and clinical conditions in the skin, lungs, GI tract, mouth, eye, and beyond to help alleviate patient suffering."

Beyond the cough, itch, pain and inflammation indications that are directly related to the activation of sensory neurons, indirect activation can set off a feedback cycle through the release of pro-inflammatory neuropeptides that promote conditions like asthma, inflammatory bowel disease, dermatitis, esophagitis, and dry eye.

Company formation

Nocion Therapeutics has raised a \$27MM Series A led by Canaan and F-Prime Capital Partners with participation from Partners Innovation Fund, and BioInnovation Capital. The capital finances the company from discovery through clinical proof of concept in patients.

Tom Beck, MD, Executive Partner at F-Prime Capital Partners, and Julie Grant, Partner at Canaan, teamed up to form and spin out Nocion. "Rolling our sleeves up with exceptional scientists to build a scientific discovery into a robust company is a sweet spot for both Canaan and F-Prime," noted Grant. "Tom and I are delighted with the progress to date and formation of an esteemed executive team, which is uniquely qualified to execute upon the promising science from Harvard and Boston Children's Hospital." Dr. Beck adds, "I have had the pleasure of working with this group of outstanding scientists for the past several years. It is truly exciting to see their work mature to the point where it can serve as the basis of this exciting new company."

Forming Nocion's initial executive team are Dr. Richard Batycky, CEO and Dr. Jim Ellis, CSO. Dr. Batycky comes to Nocion with over two decades of experience in drug development across an array of platforms, disease states and registered products, and has been with several start-ups from founding through acquisition. Most recently, he was a founder of Civitas Therapeutics where their lead asset—a novel dry powder inhalation therapy to treat motor issues in Parkinson's patients—has been approved by the FDA as Inbrija[™]. Dr. Ellis joins with over 20 years of leadership experience in drug discovery in multiple therapeutic areas, working in organizations from biotech startups to large pharma. Most recently, Dr. Ellis led GSK's Innovation Hub in Cambridge after serving as Vice President and Head of GSK's Sirtuin Discovery Performance Unit.

Working with Harvard's Office of Technology Development, Nocion was founded on an exclusive license to foundational intellectual property from Harvard University and Boston Children's Hospital to develop therapeutics.

"Innovations in how clinicians treat pain are long overdue," said Isaac Kohlberg, Harvard's Chief Technology Development Officer and Senior Associate Provost. "We're thrilled that a decadelong collaboration between researchers at Harvard University and Boston Children's Hospital has borne fruit in the form of a truly novel approach to treating neurogenic inflammation. We look forward to seeing this potential therapeutic advance toward clinical development."

Nocion closed its seed financing in the first quarter of 2018 and is in operations at LabCentral in Cambridge, Massachusetts. Nocion is currently optimizing and expanding on the initial set of small molecule candidates to select leads for multiple indications.

ABOUT NOCION

Nocion Therapeutics is a biopharmaceutical company developing novel treatments for silencing neurons. The company's platform of unique molecular entities selectively affects inflamed nociceptors. Treatment using this approach aims to provide more durable and robust local analgesic effects while minimizing numbness or paralysis and other systemic off-target effects. The company's mission is to safely alleviate suffering for millions of patients with conditions arising from activated sensory neurons. For more information, visit: www.nociontx.com.

ABOUT CANAAN

Canaan is an early stage venture capital firm that invests in entrepreneurs with visionary ideas. With \$5B under management, a diversified fund and hundreds of exits to date, we partner with entrepreneurs building the next generation of technology and healthcare companies that will transform how we live, work and thrive. To learn more about our people and our portfolio, please visit canaan.com

ABOUT F-Prime Capital Partners

F-Prime Capital is a global venture capital firm investing in life sciences, healthcare, and technology. Since 1969, F-Prime has worked closely with entrepreneurs and academics to create innovative solutions to some of the world's most significant challenges in healthcare and technology. www.fprimecapital.com.

ABOUT PARTNERS INNOVATION FUND

Partners Innovation Fund is an early-stage venture capital firm focused on commercializing technologies emerging from Partners HealthCare, a research and healthcare provider system founded by Massachusetts General Hospital and Brigham and Women's Hospital, the two principal teaching hospitals of Harvard Medical School. The fund invests in leading-edge life science technologies with the goal of bringing discoveries, inventions and innovations from Partners' pre-eminent research community to the market benefit of patients worldwide.

ABOUT BioInnovation Capital

BioInnovation Capital invests in the most promising early-stage life science companies in residence at premier co-working laboratory facilities where our partners are on-site every day. As the first investment platform to knit together a national network of shared laboratories, we have a unique position from which to invest. BIC's general partners, and our labs, are located in Cambridge MA, San Francisco CA, Durham NC, and San Diego CA. Our perspective is characterized by superb access to key innovators in academia and pharma. Our overlapping network of facilities and resources supports the formation of stellar companies from the most powerful universities, research hospitals and corporations in our sector. Please visit us at www.bio-innovation.com