NEUROCARRUS

Treating Neurodegenerative Disease and Pain Without Addiction

Highlights

Regular Updates

Founders have a strong track record of investor updates.

1. Drug candidate N-001 provides relief from acute pain in animals caused by inflammation or surgery.
2. Neurocarrus has built a pipeline of drugs using the APOLLO targeting and delivery system.

3. N-001, NL-17, N-19a treat acute, migraine and chronic pain by sensory neuron targeting.

4. The APOLLO drugs use a unique manufacturing process to discourage competitors.

5. There is a massive market for the treatment of Neurodegenerative disease and pain around the world.

6. Neurocarrus has a strong track record of non-dilutive funding from federal and state government.

7. Founder has been working in the space for 25+ years trouble shooting commercial biologicals.

8. Patents issued and pending on exclusively licensed technology in both the U.S. and select countries.

Team

Paul Blum Co-founder/CEO

30+ years in cell engineering and microbiology, focused on protein drug development. Paul is full time CEO of Neurocarrus in Monterey, California. He is a serial inventor and was an endowed university professor.

Derek Allen Research Scientist

Ph.D. focused on protein drug development with emphasis on protein synthesis and purification. Also specialized in bioassays and potency studies.

Jianguo Cheng, MD, Ph.D Board Member

Professor and Director, Cleveland Clinic; Past President, American Academy of Pain Medicine. Highly active in research and pain medicine and strongly supported by NIH. Also an active editor in top pain journals.

Bruce McDonald, JD Board Member

Partner in the intellectual property group at Smith, Gambrell & Russell, LLP; member of the District of Columbia Bar. Specialized in trademark law and intellectual property litigation, particularly negotiation of licensing agreements.

Mark Blum, JD Board Member

Mark is an attorney licensed in California who practices law in California since 1986. For the past three years, he has continued his role as a shareholder, managing member and practicing attorney at Horan Lloyd.

Vicky Valverde Salas Board Member

Vicky attended MIT majoring in Mathematics, Physics and Biology. He earned an M.D. from the U. Madison Wisconsin Medical School and trained in Family Medicine at Case Western Reserve. For the past 20 years he ran his own medical Primary Care Clinic.

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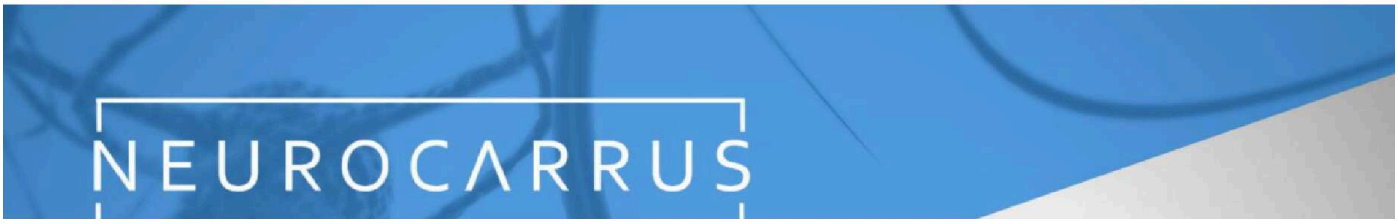
Publications:

Neurocarrus top scientific publications:

Animal efficacy and safety studies

Targeting, mechanism, and efficacy studies

Drug design and engineering studies



Welcome to Neurocarrus!

We are a drug development startup company making a new therapeutic to treat severe human pain without addiction.

Paul Blum our CEO, invented the drug while at the U Nebraska. After retiring from academia, he now works full time at Neurocarrus.

Together with chief scientist Derek Allen and other Neurocarrus staff, our team is highly motivated to bring our drug to market.

Help us fight the opioid epidemic and solve the human tragedy of widespread poorly managed severe pain.

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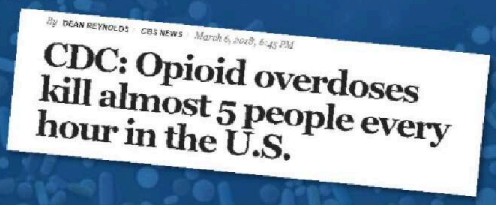
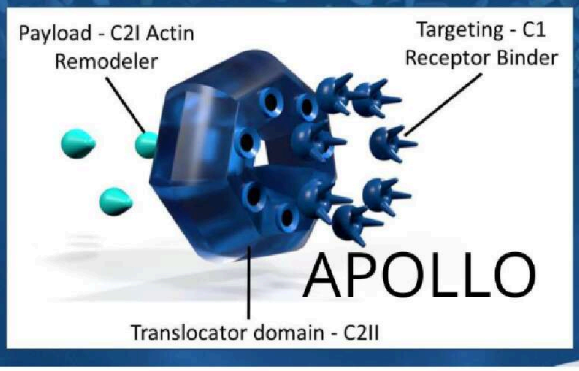
Current drugs for neurodegenerative disease and severe pain can be addictive and toxic resulting in hundreds of thousands of deaths per year



Neurocarrus designed APOLLO as a novel drug delivery platform for treatment of diverse neurodegenerative disease without addiction, toxicity or off-target effects



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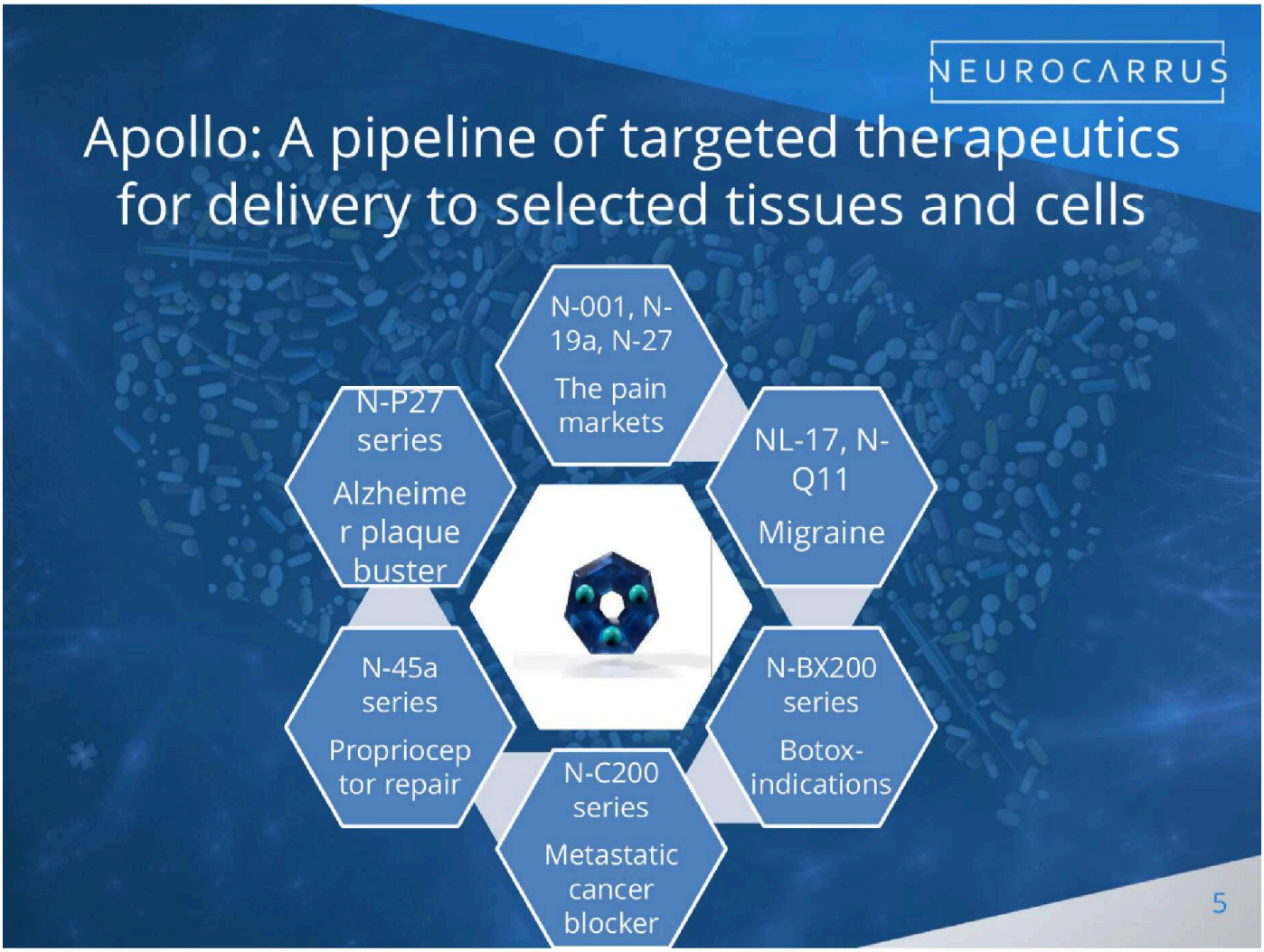
Neurodegeneration and Pain:
Neurodegeneration damages neurons and often causes pain (called sensory neurons) that lie outside the central nervous system and brain. Therefore the Neurocarrus drug, N-001, designed using the APOLLO targeting and delivery system finds and attaches to such neurons located only in the body's peripheral regions (not brain) and then calms their excessive activity. This strategy avoids addiction because it avoids the central nervous system (brain).

To target sensory neurons and and treat pain, N-001 had to be multi-functional. N-001 is targeted to sensory neurons not motor neurons and therefore has no effect on muscles. It is only active once it goes inside sensory neurons. Together these two functions limit side effects and

distinguishes N-001 from all other pain drugs. Once inside the sensory neuron, N-001 modifies the internal actin-based skeleton to reduce neural signaling.

The Neurocarrus drug acts like a dimmer switch on neurons without blocking sensation. Importantly N-001 is reversible.



A pipeline of new therapeutics :

Using the APOLLO targeting and delivery system, a deep tech invention unparralelled in pharmaceutical science, Neurocarrus has built a series of candidate therapeutics.

N-001 treats acute pain
NL-17 treates migraine
N -19a treats chronic pain

Each of these biologics (proteins) have unique medical uses for specific populations providing important value propositions.

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Leading Drug Products are Efficacious, Safe and Valuable

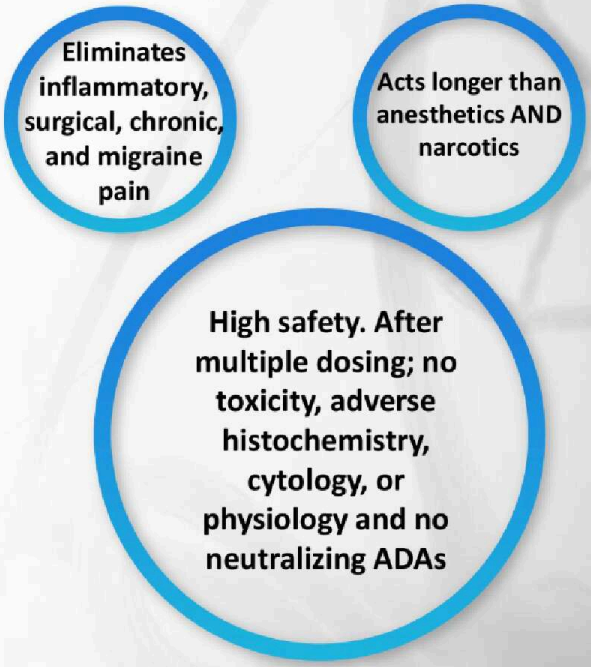
Main Indications

Acute Pain asset N-001: at a price point of $500 per dose (estimate based on competitor anesthesia) this is market entry at **$250M revenue** with capacity to expand 100 fold and **net profit of $200 per dose**.

Chronic pain asset N-19a: 1% market entry (670K patients) dosed monthly **$4.02B revenue** per year.

Migraine Prevention asset NL-17: 1% market entry (66K patients) dosed monthly is **$396M revenue** per year.

Preclinical PAIN Trial Metrics*



*Independently confirmed by CROs and Stanford University using double blinded procedures

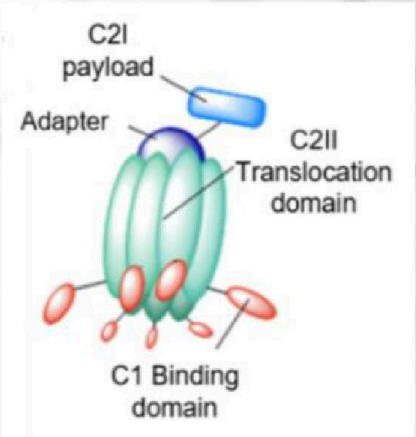
Alternatives and Competitors

N-001 is first-in-class

	N-001	Opioids (OxyContin)	Over-the-counter (Tylenol, Ibuprofen)	Anesthesia (Amytal)	Long Lasting Anesthesia (Exparel)
Severe Pain Surgical	X	X		X	X
Non-addictive	X		X	X	X
Long lasting	X				X
Targeted	X				

N-001 Profile

- A rationally designed multifunctional biological (protein) that targets sensory neurons and is active only inside them.
- Cell targeting combined with intracellular activity minimizes side effects and improves likelihood of positive clinical trial outcomes.
- Locally administered at the site of pain, by injection or patch or nerve block, not systemic no CNS effect.
- Preclinical tests measuring efficacy and safety are promising.



The market opportunity and human health:
With an estimated 30% of the population worldwide affected, pain is one the most prevalent health problems in the world. Pain is affecting 56% of American adults, more than diabetes, heart disease, and cancer combined.

Acute pain due to injuries, accidents, labor, and childbirth, or surgeries represents a significant concern for 67.5% of patients admitted to hospitals. There are nearly 50 million surgeries in the US per year that involve pain management.

Unrelieved acute pain is one of the risk factors in the development of chronic pain, with 10% - 50% of patients developing persistent pain after different operations. Specifically, there are over a million orthopedic surgeries performed each year in the US. Total hip and knee arthroplasties are common surgeries in orthopedics with more than 300,000 hip replacements and 600,000 knee replacements performed each year.

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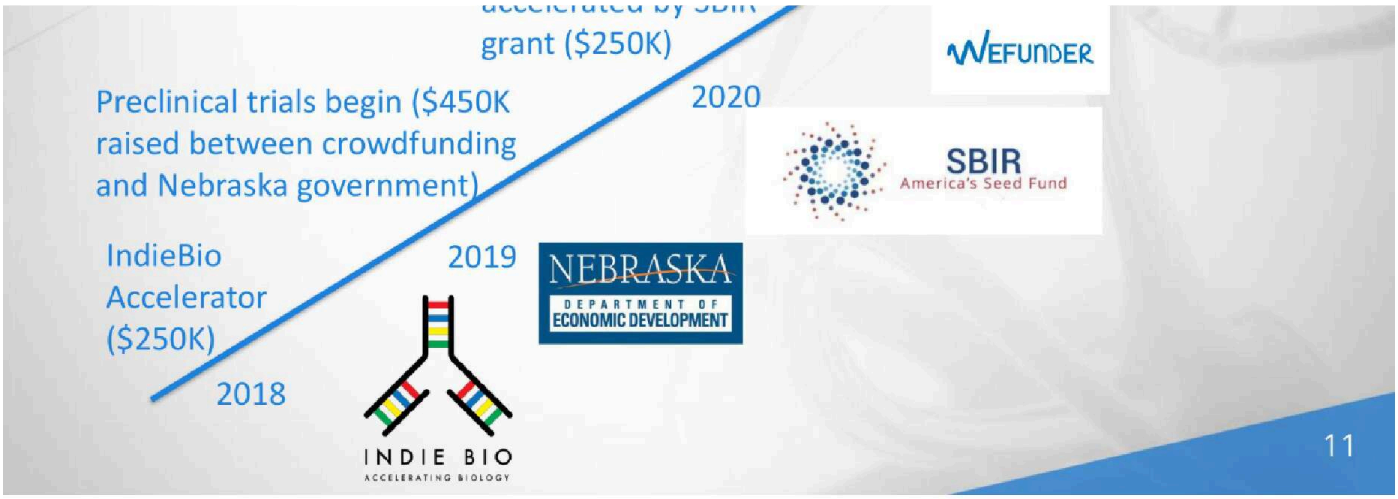
Progress

Neurocarrus progress is accelerating



A history of strong funding:
Neurocarrus has received considerable non dilutive investment ($3,321,000). These federal and state awards result from confidential reviews by pain experts and business executives coordinated by the awarding sources. They prove that Neurocarrus is highly competitive within the landscape of the US medical establishment. The company has received $600,000 in private investment resulting in a very promising ratio of 5.6 non-dilutive to dilutive funding for future investors. This means that their investment leverages the much larger federal and state commitments which dictate valuation.

A well developed commercialization plan:
Our current Phase II NIH SBIR award of $2,780,000 depended on development of a highly detailed commercialization plan that was reviewed and vetted by reviewers. This plan includes near and long term strategies to develop N-001 within the structure of the federal approval process and to fund the development by strategic partnerships.

And now opportunities to out-license pipeline drugs for revenue generation

Accomplishments Since Our Last Wefunder Raise

NEUROCARRUS

Before Wefunder Raise

After Wefunder Raise

IndieBio Incubator Class 6

Public Dissemination: First publication: https://doi.org/10.1038/srep23707

$100K non dilutive funding awarded by Nebraska Department of Economic Development.

2020:
$250K non dilutive funding awarded by the US NIH Phase I SBIR program

$91K non dilutive funding awarded by Nebraska Department of Economic Development

Partnered with Stanford Medical School and Veterans Administration in Palo Alto CA

First U.S. patent issued

Public Dissemination: Second publication: https://doi.org/10.1038/s41598-020-69612-9

2021:
Accepted into the United States NIH Preclinical Screening Platform for Pain

Second U.S. patent issued

2023:
$2.78M non dilutive funding awarded by the NIH Phase II SBIR program

$100K non dilutive funding awarded by Nebraska Department of Economic Development

Public Transparency: Third publication: https://doi.org/10.1038/s41598-020-69612-9

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Investor Opportunity and Exit Strategies

Wefunder investors receive a SAFE in exchange for their investment using a contract between the investor and Wefunder. A SAFE is a Simple Agreement for Future Equity and is like a convertible note but less complicated. When conditions are met such as an Equity Financing of preferred stock, SAFEs convert to preferred stock.

Investors have several potential strategies to make money. Neurocarrus may be acquired and the investor's shares would be bought out at an increased valuation in exchange for cash, or potentially exchanged for shares in the purchasing company. Alternatively, Neurocarrus may go public and undergo an initial public offering (IPO) allowing investor shares to be publically traded and sold.

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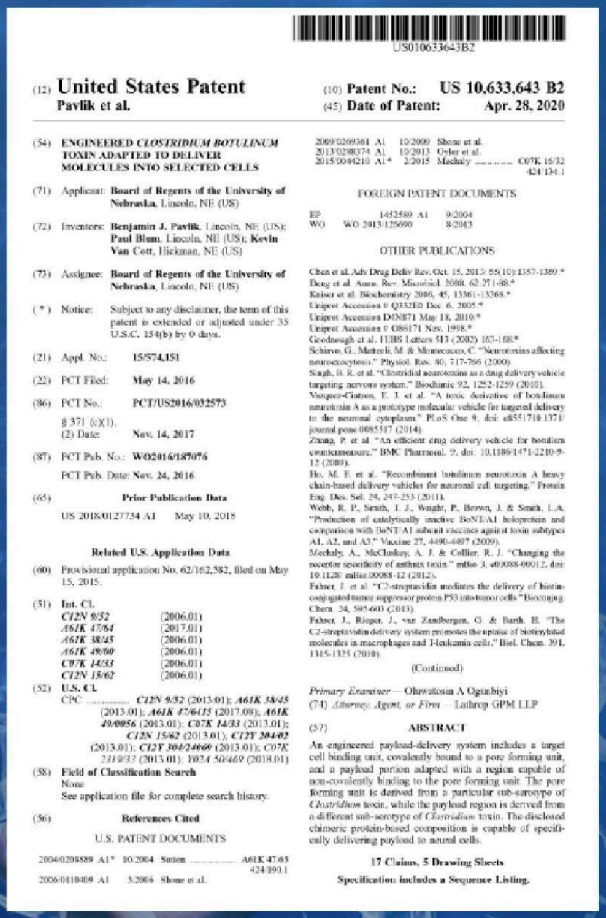
Intellectual Property



US010633643B2

(12) **United States Patent**
Pavlik et al.

(10) **Patent No.: US 10,633,643 B2**
(45) **Date of Patent: Apr. 28, 2020**

(54) **ENGINEERED *CLOSTRIDIUM BOTULINUM* TOXIN ADAPTED TO DELIVER MOLECULES INTO SELECTED CELLS**

(71) Applicant: **Board of Regents of the University of Nebraska**, Lincoln, NE (US)

(72) Inventors: **Benjamin J. Pavlik**, Lincoln, NE (US); **Paul Blum**, Lincoln, NE (US); **Kevin Van Cott**, Hickman, NE (US)

(73) Assignee: **Board of Regents of the University of Nebraska**, Lincoln, NE (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/574,151**

(22) PCT Filed: **May 14, 2016**

(86) PCT No.: **PCT/US2016/032573**
§ 371 (c)(1),
(2) Date: **Nov. 14, 2017**

(87) PCT Pub. No.: **WO2016/187076**
PCT Pub. Date: **Nov. 24, 2016**

(65) **Prior Publication Data**
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Related U.S. Application Data

(60) Provisional application No. 62/162,582, filed on May 15, 2015.

(51) **Int. Cl.**

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A61K 47/64	(2017.01)
A61K 38/45	(2006.01)
A61K 49/00	(2006.01)
C07K 14/33	(2006.01)
C12N 15/62	(2006.01)

(52) **U.S. Cl.**
CPC ***C12N 9/52*** (2013.01); ***A61K 38/45*** (2013.01); ***A61K 47/6415*** (2017.08); ***A61K 49/0056*** (2013.01); ***C07K 14/33*** (2013.01); ***C12N 15/62*** (2013.01); ***C12Y 304/24*** (2013.01); ***C12Y 304/24069*** (2013.01); *C07K 2319/33* (2013.01); *Y02A 50/469* (2018.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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(Continued)

Primary Examiner — Oluwatosin A Ogunbiyi
(74) *Attorney, Agent, or Firm* — Lathrop GPM LLP

(57) **ABSTRACT**

An engineered payload-delivery system includes a target cell binding unit, covalently bound to a pore forming unit, and a payload portion adapted with a region capable of non-covalently binding to the pore forming unit. The pore forming unit is derived from a particular sub-serotype of *Clostridium* toxin, while the payload region is derived from a different sub-serotype of *Clostridium* toxin. The disclosed chimeric protein-based composition is capable of specifically delivering payload to neural cells.

17 Claims, 5 Drawing Sheets
Specification includes a Sequence Listing.

- Patent No. 10,633,643 issued by USPTO on April 28, 2020 (priority date in 2015)
- Follow on divisional Patent No. 11,118,170 issued May 19, 2021
- Neurocarrus exclusively licensed these patents for all-fields-of-use along with a sublicense option.
- PCT US 1632573 has issued in Japan 2017-559588 (6-17-21) and EU and is pending in Canada, Israel, and South Korea.
- Provisional 63/695,737 filed September 2024 for treatment of Migraine – extends IP sales protection to 2044
- Provisional filing anticipated 2025 for treatment of chronic pain

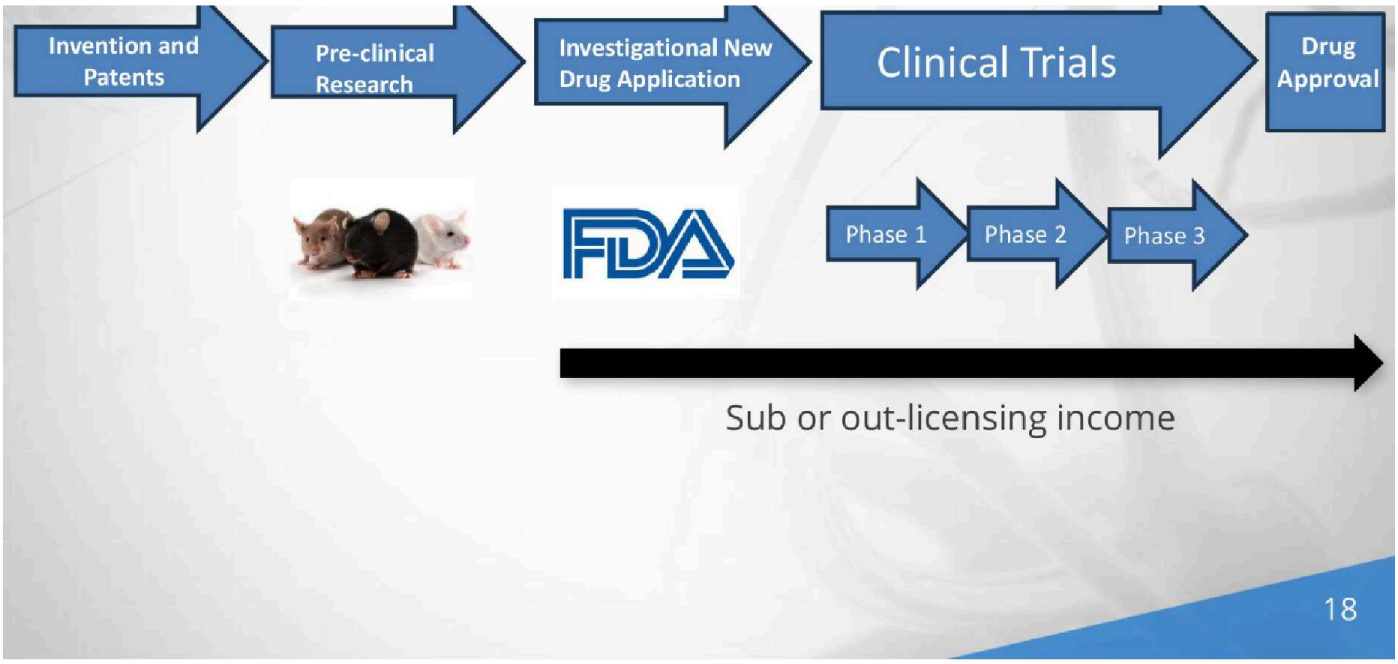
What does success look like?
Solving severe pain without addiction is its own reward. Financial benefit to early investors will result in part from the ongoing protection of intellectual property.

Neurocarrus has two issued US patents invented by CEO Paul Blum and coworkers. The company continues to pursue protection of its intellectual property by patent protection in other countries. These countries were selected by their current manufacturing ability to make protein drugs. Fortunately, the Covid epidemic revealed and reinforced as highly strategic, the selection of countries made by Neurocarrus.

Neurocarrus recently filed a new patent about migraine

Neurocarrus recently filed a new patent about migraine treatment using NL-17, extending the period of protected drug sales and increasing interest by long term investors.

Neurocarrus will continue its aggressive IP strategy to extend protection of its inventions.



Neurocarrus is early stage in its drug development process:
The company's studies are "pre-clinical" meaning before testing in humans. Some of these studies are described in our publications and many more are underway. The Phase II SBIR award indicates the company has made very significant progress and intends to pursue clinical trials at the end of the funding period.

Preclinical testing uses animals to ensure drug benefit and safety before human testing. While the company regrets the dependence on using animals there are no alternatives. However, all attempts are made to minimize this testing and federal guidelines are followed closely in these efforts.

After pre-clinical development and approval of an IND (application for investigative drug), human testing, called clinical trials occur. They are divided into three stages, phase I, II and III. Each of these trials focus on specific outcomes, safety then benefit then more safety and benefit. Clinical trials are expensive. Funding will be pursued from multiple sources including the federal government by grants, from private investors and from strategic partnerships.

Finally, approval for distribution and sales of N-001 will be pursued in concert with pharmaceutical companies to benefit from their marketing and distribution networks.

The Neurocarrus team:
Paul Blum, CEO of the company has over 30 years of research experience in protein engineering and microbiology. He leads a multidisciplinary team of investigators including chief scientist Derek Allen, with complementary expertise in pain physiology, protein biochemistry, pharmacology, microscopy, and commercial preclinical drug development.

Continuing efforts to establish drug benefit are led by Stanford University's Dr. David Clark, an expert in post-traumatic chronic pain and pain relief pathways. In addition, the company benefits from widespread interest among scientists and the public in the improvement of pain management.

The Neurocarrus advisory board currently includes doctors and lawyers with a history of interest in human pain and the development of Neurocarrus. Additional members of the company include other scientists and lawyers. Pending new federal funding may add a salaried CEO to the Neurocarrus team to raise private

capital and to coordinate strategic deals.

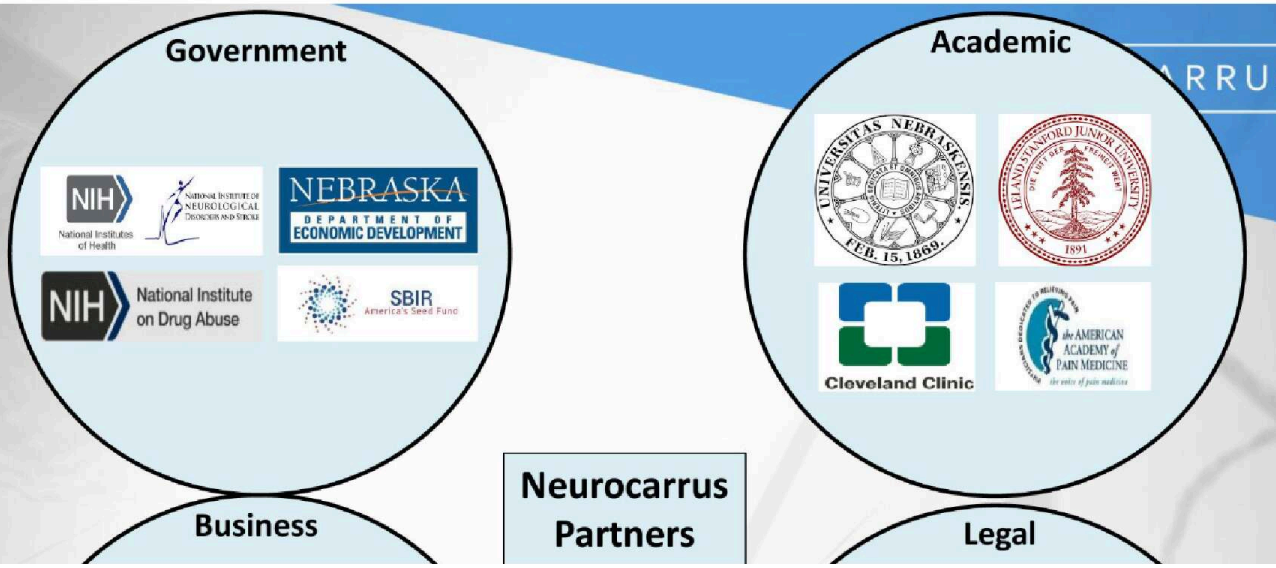
Advisors and collaborators

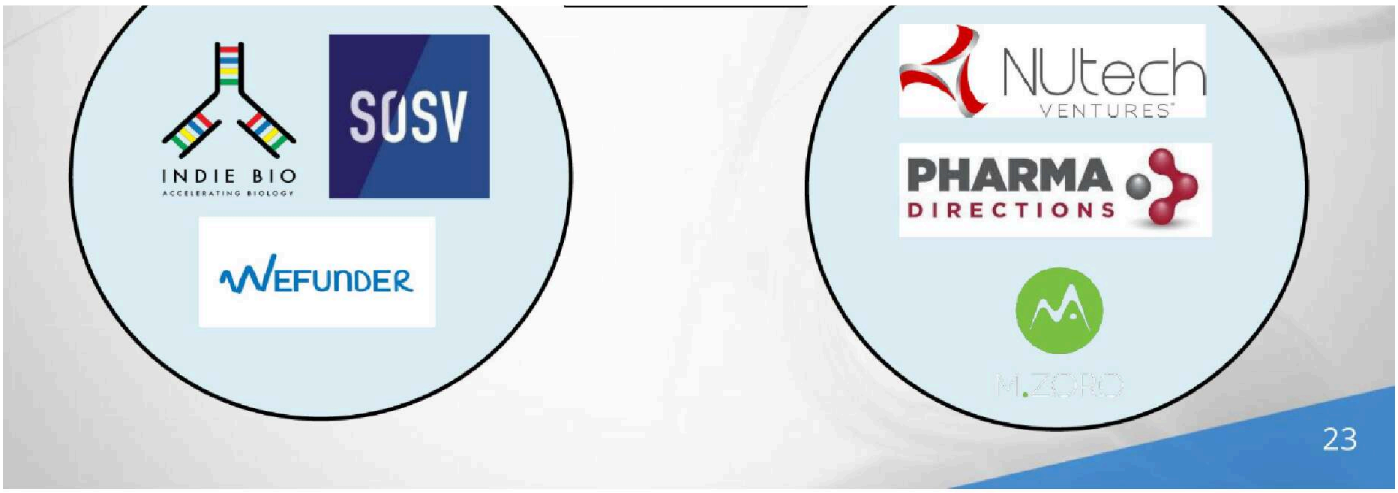
NEUROCARRUS

David Clark, MD., Ph.D. *Pain Specialist Advisor and Collaborator* Director of pain relief service, VAPHCS; Professor of anesthesiology, perioperative, and pain medicine at Stanford Medical Center; Member of Bio-X, Member of Wu Tsai Neurosciences Institute; 30 years' experience in pain research.

Rebecca Wachs, Ph.D., M.Eng., *Chronic Pain Specialist Advisor and Collaborator* Assistant Professor of Biological Systems Engineering Graduate Chair University of Nebraska-Lincoln

You Zhou, Ph.D., *Microscopy Advisor and Collaborator* Research Professor University of Nebraska-Lincoln; Director of UNL microscopy research core facility

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