



ten zero
biosciences

Novel therapeutics targeting intractable neuropathic pain

Nonconfidential Overview



TenZero develops non-opioid, small-molecule therapeutics that address novel neuropathic pain targets, identified directly from pain-causal human spinal cord tissue



Investment Thesis

Neuropathic Pain (NP) Market Is Large

- 26M American adults: ~10% prevalence
- 17% of NP patients report their pain as “worse than death”
- \$46K per patient annual cost for patients with severe NP
- Multiple, \$1B+ indications with commercial precedents (Lyrica, Neurontin)

Compelling Unmet Medical Need

- Approved therapies (e.g., Lyrica) fail most patients
- Opioids used despite ineffectiveness, addiction & overdose
- Few novel agents in clinical development
- Lack of novel, validated targets represents a key bottleneck

Proprietary HNP³ Platform

- *Human* Neuropathic Pain Proteome Platform (HNP³)
- Avoids false leads from rodent models
- Unique resource: Falci Institute surgical biopsies of human pain-causal spinal cord tissue (exclusive access)
- Proteomic analyses of pain-causal spinal cord tissue to support target identification
- Prioritized portfolio of ~60 initial targets with opportunity for expansion

Platform Validation

- SV2A identified as a pain target among the ~60 initial targets
- Briviact targets SV2A
 - FDA-approved as anti-seizure medication (no pain indication)
- Significant reduction of severe NP in a placebo-controlled Phase I/II study
- *POC only – not a repurposing play*

Discovery Programs

- Pursuing three multi-target initiatives
 - GPCR function (4 targets)
 - Ion channels (1 target)
 - Synapse Modulation (3 targets)
- Complementary MOAs across programs
- Poised to begin hit discovery
- Targeting two INDs in first 5 years

Experienced Leadership Team and Board



Scott Falci, MD

Chief Executive Officer, Director

Founder – TenZero, Founder – Falci Institute
Board certified neurosurgery



Larry Gold, PhD

Chairman

SomaLogic (acquired), NeXstar (acquired),
NeXagen, Synergen (acquired), University of Colorado



Todd Gander, MBA

Chief Business Officer

Biodesix, Medtronic, Replidyne, SomaLogic,
NeXstar, Empire BC/BS, BCG



Kirk Christoffersen, MBA

Director

FibroGen, Arch, Compugen, Globelimmune,
OSI Pharma, Gilead, NeXstar



Lawrence Hunter, PhD

Chief Technology Officer

University of Chicago, NIH,
Founder - International Society
for Computational Biology



Allan Jacobson, PhD

Director

PTC Therapeutics, Applied Biotechnology,
UMass Chan Medical School



John Swindle, PhD

Chief Scientific Officer

SomaLogic, CompleGen, Seattle Biomedical
Research Institute, University of Tennessee



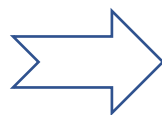
Nebojsa Janjic, PhD

Director

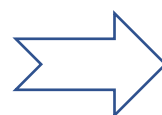
Crestone, SomaLogic, Replidyne,
NeXstar, NeXagen

TenZero Has Leveraged HNP³ to Identify Novel Targets

Causal
Tissue



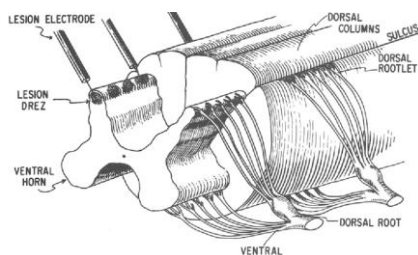
Causal
Proteins



Proofs of
Concept

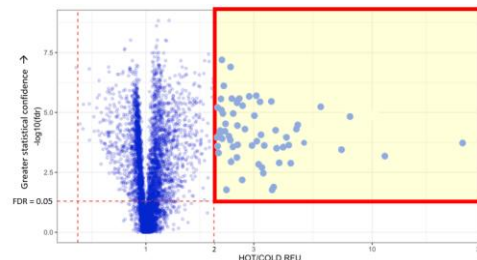


Drug
Discovery

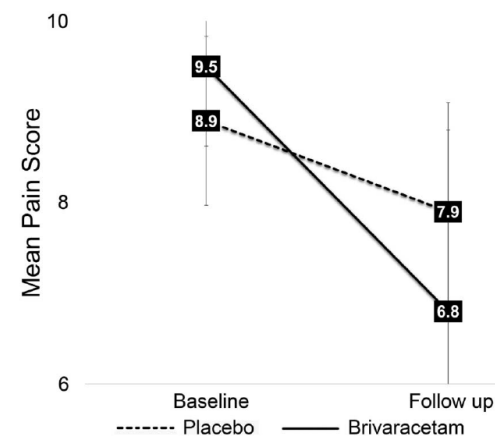


Proprietary tissue bank: surgical biopsies of human pain-causal spinal cord tissue for proteomic analysis

The Red Box



Identifying proteins that drive neuropathic pain – definitive portfolio of human neuropathic pain targets



Platform validation in placebo-controlled study with FDA-approved drug

**Novel Therapeutics
for
Neuropathic Pain**

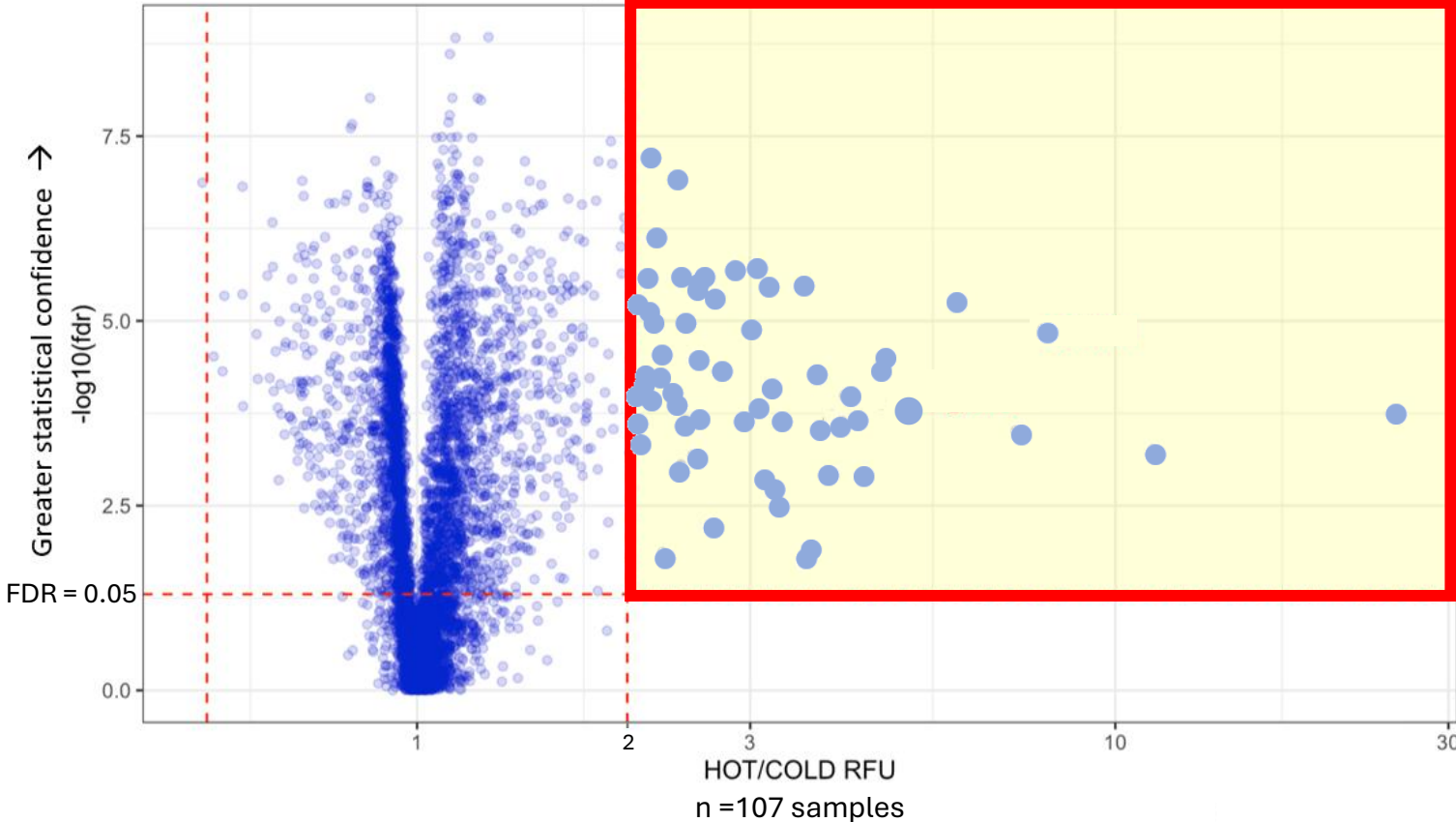
Human Neuropathic Pain Proteome Platform (HNP³) Unlocks Novel Neuropathic Pain Targets

- Spinal cord injury (SCI) patients often experience severe neuropathic pain in regions devoid of sensation
 - Generally refractory to available drugs
- Surgical insight: Electrical hyperactivity in dorsal root entry zones (DREZs) drives SCI pain
 - Essentially epilepsy of the spinal cord
 - Only the Falci Institute performs DREZ surgery with intramedullary electrophysiological guidance, leading to a unique collection of pain-causal human spinal cord tissue biopsies
 - Ablating electrically hyperactive (“hot”) pain-causal DREZs brings complete relief to 85% of patients
 - TenZero has exclusive access to the Falci Institute’s pain-causal spinal cord tissue biopsies
- Neuropathic pain target discovery
 - Goal: identify differentially abundant proteins in pain-causal tissue → potential drug targets
 - Core data: quantitative proteomic analysis of ~5,000 proteins in 54 pain-causal and 53 same-patient control DREZ biopsy samples (10 subjects, IRB-approved protocol)
 - Integrated with other protein-focused data and deep analysis to support target prioritization

Result: Initial set of ~60 novel, unexploited neuropathic pain targets

Novel Targets Identified in Hot vs. Cold Tissue by Proteomic Analysis

Increasing protein abundance in electrically hyperactive tissue →



SOMAscan 5K
Measurement of ~5,000 proteins

Red Box
~60 proteins $\geq 2x$ over-abundant in pain-causal (hot) vs. control (cold) tissue with FDR < 0.05

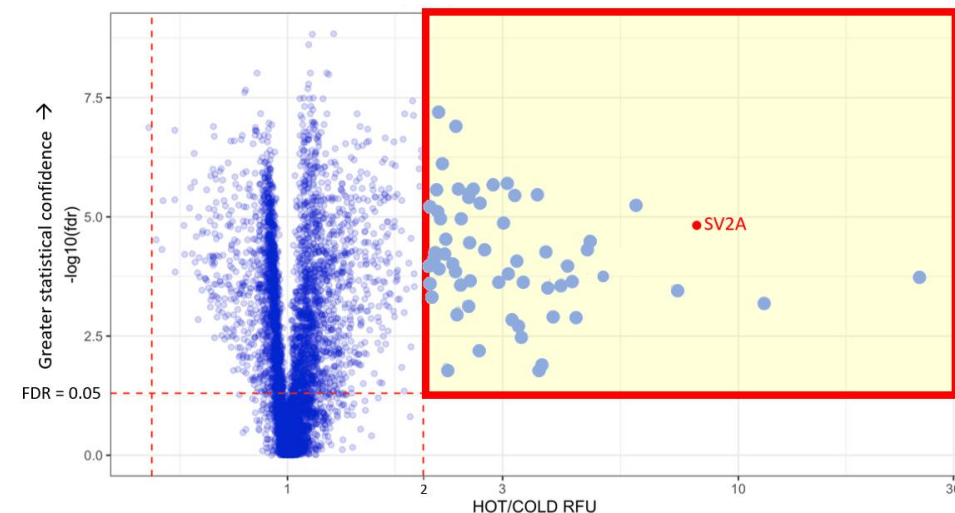
Potential Expansion
110 additional proteins $\geq 1.5x$ over-abundant

Each dot represents one protein across all patients and samples;
FDR = false discovery rate, a measure of statistical significance

Platform Validation: SV2A Targeted by Brivaracetam

TenZero is not pursuing brivaracetam drug repurposing

- SV2A: synaptic vesicle glycoprotein 2A
 - Enhanced expression in neuronal cells
 - Positively regulates vesicle fusion
- SV2A proteomic analysis – Red Box protein
 - 8.1x over-abundant in pain causal tissue (Hot:Cold)
 - FDR = 1.5×10^{-5} (significant finding)
- Brivaracetam approved for the treatment of epilepsy
- Clinical proof-of-concept for HNP³ target identification
- TenZero Programs target other HNP³-identified targets

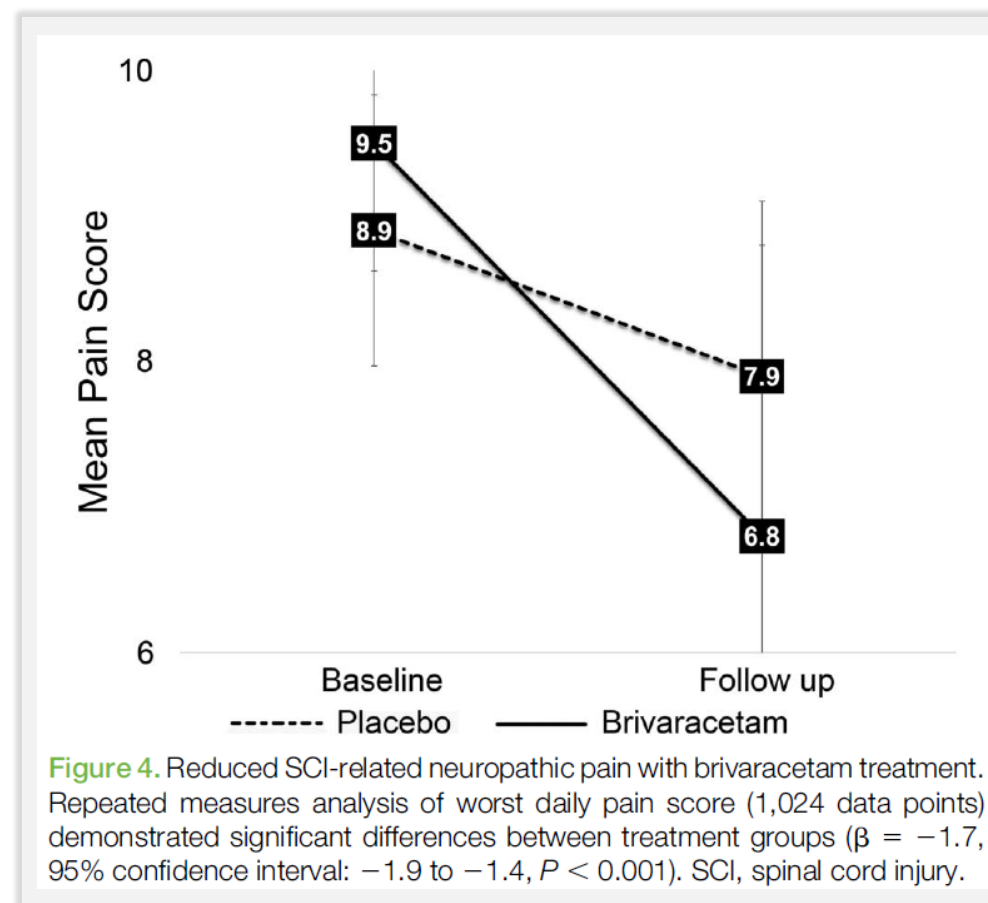


Platform POC: Brivaracetam Clinical Trial

Targeting SV2A brought relief to patients suffering from intractable spinal cord injury neuropathic pain

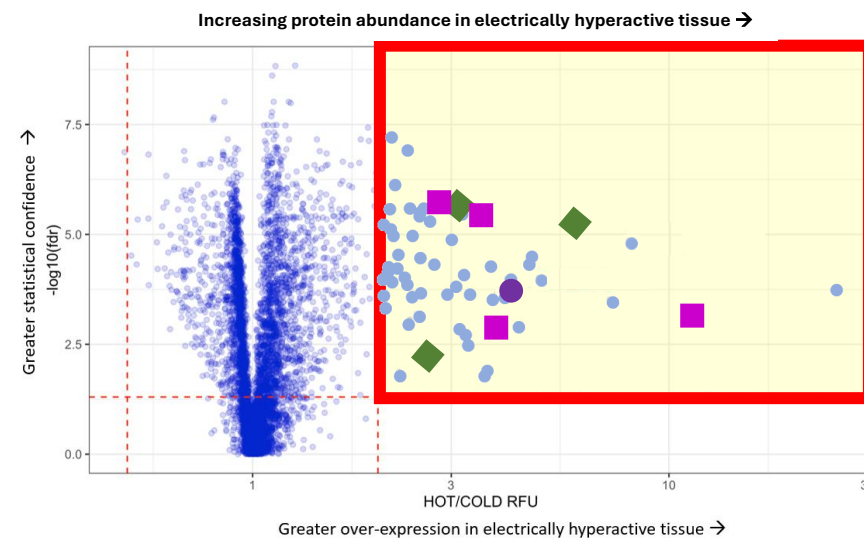
SV2A validated by significant reduction in worst daily pain score with brivaracetam

- Phase 1/2 placebo-controlled study (N=24)
 - Patients with severe (9/10 to 10/10) spinal cord injury-related neuropathic pain
 - Endpoint: Change in pain (0-10 scale)
 - Duration: three months
 - Analysis set: 14 subjects completed study (8 placebo, 6 brivaracetam)
- Briviact-treated patients demonstrated an average **2.7-point** improvement in worst daily pain score vs. 1.0-point change with placebo
- **Platform Validation: confirms SV2A as validated pain target identified with HNP³**



Discovery Programs: Pursuing Eight Targets Across Three Target Classes

- Program 1: GPCR function (4 targets) ■
- Program 2: Ion channel (1 target) ●
- Program 3: Synapse modulation (3 targets) ◆
- Potential for complementary MOAs among programs
- Lead indication: spinal cord injury-associated neuropathic pain
- Rigorous criteria for down-selecting to two clinical candidates
- Target two INDs within five years of funding



SCI Pain – Strategic Entry Point for Multiple NP Indications

Clinical experience and neurobiology suggest common mechanism

| Neuropathic Pain Indication | Small Fiber Loss/ Deafferentation (c-fiber) | Sympathetic Mediation | Refractory to Opioids |
|--|---|--------------------------|--------------------------|
| Spinal cord injury-associated neuropathic pain | ✓ | ✓ | ✓ |
| Diabetes peripheral neuropathic pain | ✓ | ✓ | ✓ |
| Fibromyalgia | ✓ | ✓ | ✓ |

Causal proteins in electrically hyperactive DREZ in SCI patients are potentially relevant for a broad range of neuropathic pain indications

Life Cycle Management: Multiple \$1B+ Indications

Overall community prevalence of neuropathic pain in the United States estimated at 9.8%

Market Analysis by Indication

Annual revenue per patient (uniform across indications)¹

\$5,000 - \$15,000

| | Spinal Cord Injury Neuropathic Pain | Fibromyalgia | Painful Diabetic Neuropathy |
|--|--|--------------------------|--------------------------------|
| Prevalence of Underlying Condition | | | |
| North America | 315,729 | 7,476,500 | 30,038,216 |
| W Europe | 174,146 | 8,778,836 | 20,856,982 |
| Japan | 65,298 | 2,614,409 | 5,997,725 |
| Australia & New Zealand | 12,764 | 628,769 | 1,265,560 |
| Total | 567,937 | 19,498,514 | 58,158,483 |
| Proportion with moderate to severe neuropathic pain | 65% | 25% | 10% |
| Proportion without substantial reduction in NP (≥50%) with Lyrica ² | 74% | 76% | 59% |
| Eligible Pts | 273,178 | 3,630,623 | 3,431,350 |
| TAM | \$1.4B - \$4.1B | \$18.2B - \$54.5B | \$17.2B - \$51.5B |

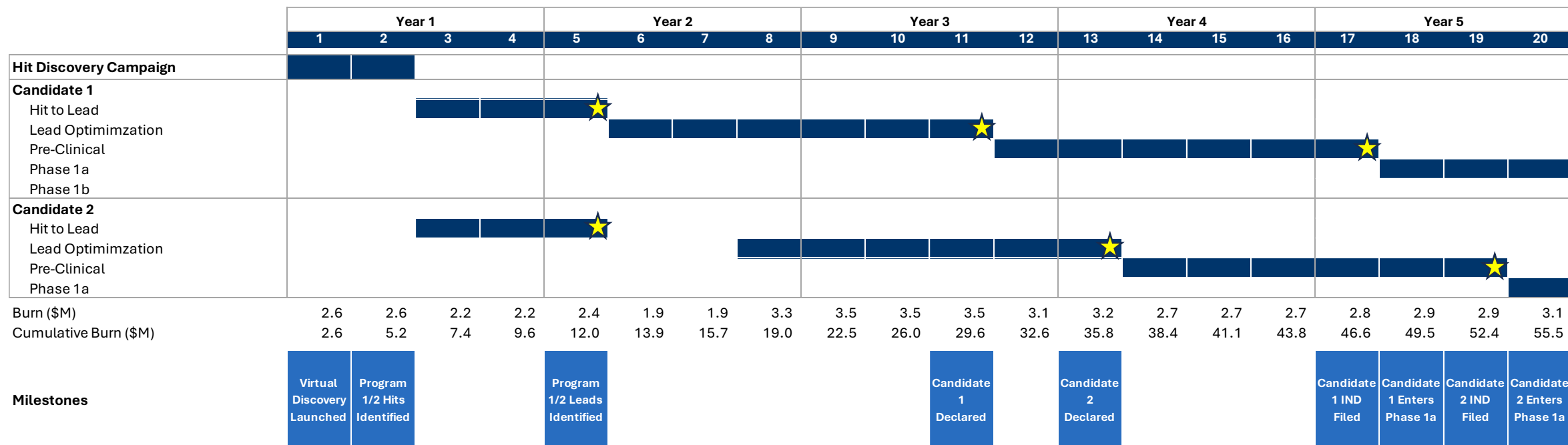
¹ Vertex's Journavx launched in January 2025 with annual pricing of \$11,315 for chronic therapy (list price)

² Based on gross percentage achieving substantial benefit in Cochrane Reviews, *not* adjusted for placebo effect.

\$15M Seed Round: Two Lead Candidates Identified

\$60M Total to File 2 INDs, For 2 NCEs, Against Novel Pain Targets

- Advance two novel pain drugs into early clinical development
 - Product 1: Candidate declared Q3 of Year 3; IND filing Q1 of Year 5
 - Product 2: Candidate declared Q1 of Year 4; IND filing Q3 of Year 5
 - Lead indication: spinal cord injury-associated neuropathic pain (Phases 1a/1b will be collapsed if possible)
- Build out team to support execution plan



★ = Value inflection point



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