Six Therapeutics

# First-to-market TLR9 Agonist To Harness The Immune System And Accelerate Wound Healing

NON-CONFIDENTIAL

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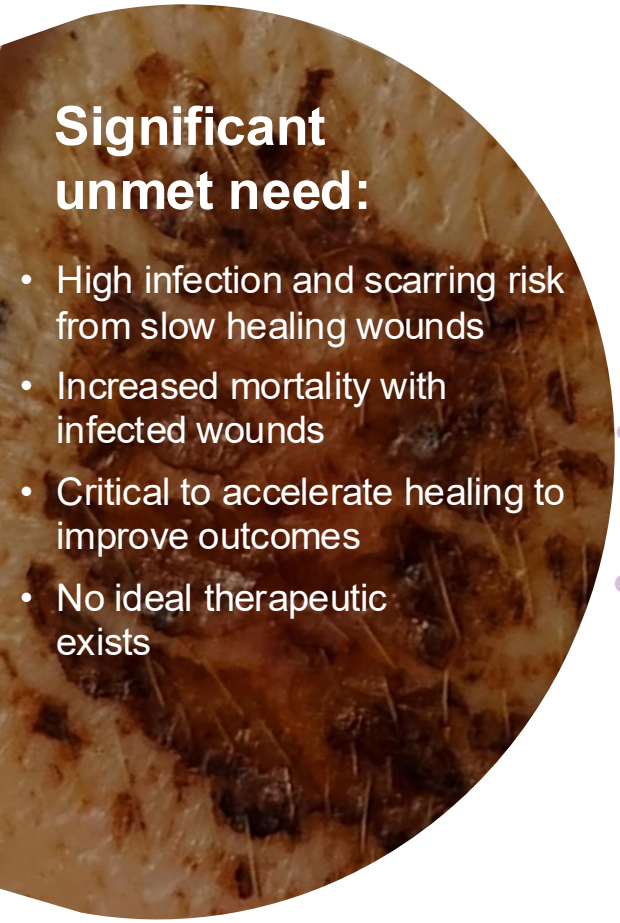
# First-to-Market Product In Wound Healing; Massive Commercial Potential; Derisked Development Path



## Significant unmet need:

- High infection and scarring risk from slow healing wounds
- Increased mortality with infected wounds
- Critical to accelerate healing to improve outcomes
- No ideal therapeutic exists

## Novel, First-to-Market Solution

- First TLR9 agonist in wound healing
- Immune stimulating MOA leads to accelerated healing
- Initial target indication for treatment of deep acute wounds (e.g. surgical)
- Data generated demonstrates safety and efficacy in target indication with clinically relevant models
- Class level safety demonstrated in >12,000 patients
- US patent 12,344,846B2 issued July 2025

## Straightforward Derisked, Execution

- Safety demonstrated at product and class level
- Rapid clinical execution:
  - FDA guidance provides clear, straightforward development path
  - Large, uncomplicated patient population
  - Short study duration
  - Done in outpatient setting
- Low total cost from development to commercial approval

## Investment Being Sought:

**$3.5 M**

Provides runway for 1.5 years to fund IND-enabling studies and secure approval to begin clinical trials

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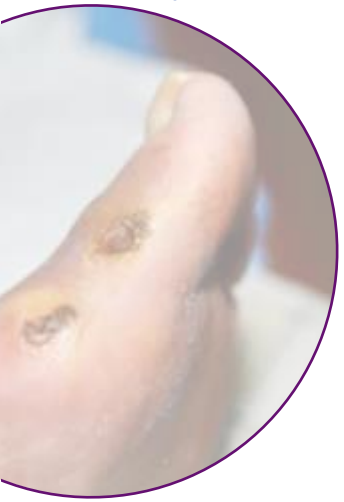
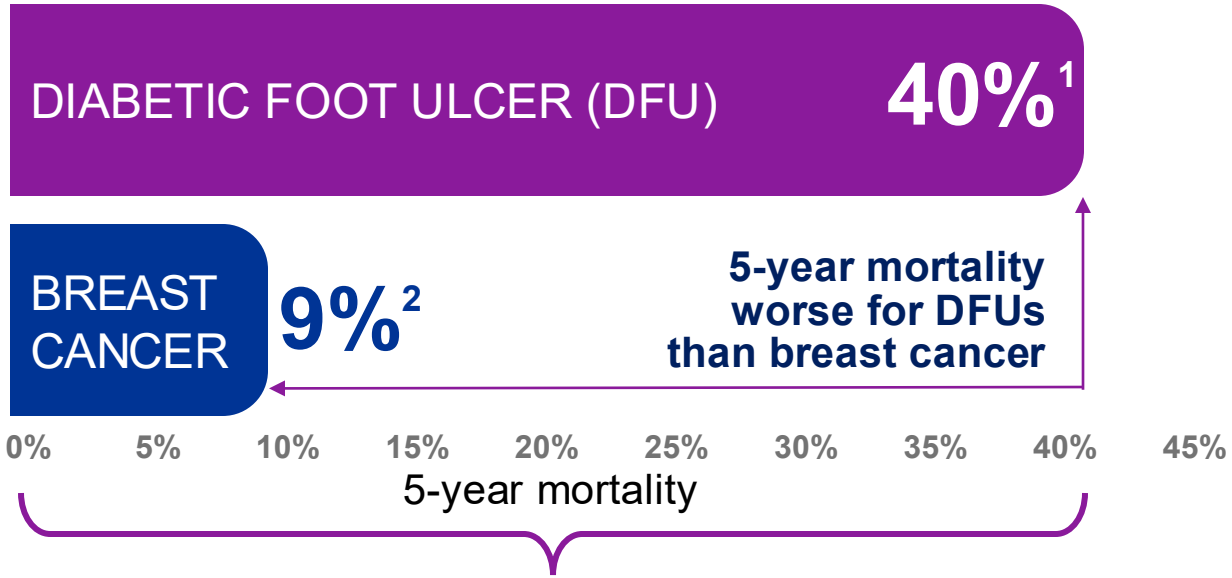
# Wounds Are A Major Healthcare Challenge With Poor Mortality And High Costs

## Infections and delayed healing are key drivers:

### Chronic wounds (e.g. DFU)






**Annual cost: $80B[1]**

### Acute wounds (e.g. surgical wounds):

**5x Mortality Risk**

Patients with surgical infections 5x more likely to die[3]

**$3B Annual Cost[4]**

**Critical to accelerate healing to prevent infections, improve mortality and reduce costs**


1. Armstrong, Journal of Foot and Ankle Research 2020, 13:16
2. American Cancer Society Breast Cancer web page Wan BJS, 2021, 108, 220–227
3. Wan. BJS. 2021. 108. 220-22
4. Zabagio, StatPearls [Internet}, 2024

# No Ideal Wound Healing Therapeutic Exists; Our Goal Is To Fill This Gap

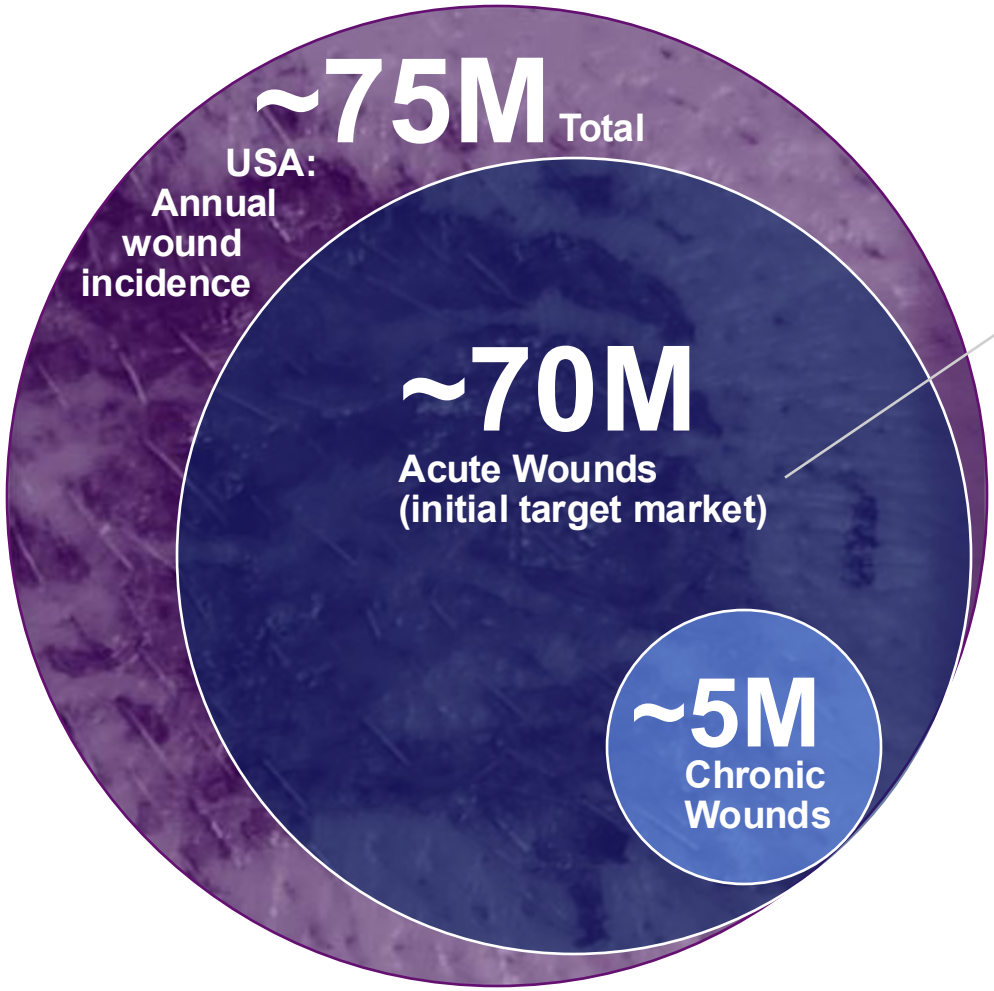
**Our first-to-market, topically applied, immune-stimulating product meets all the clinical needs required to be a frontline option:**

| | TOPICALS | NON TOPICALS | Six Therapeutics CANDIDATE |
|---|---|---|---|
| EFFICACY | − | + | + |
| SAFETY | + | − | + |
| CONVENIENCE | + | − | + |
| COST | + | − | + |

*"…The reality is that **no single therapeutic today reliably optimizes healing** across all wound types…we need a paradigm shift: smarter technologies that address the unique biochemistry of each wound. **Until then, patients will continue facing preventable complications, longer recoveries, and scarring.** The goal isn't just to heal wounds—it's to restore function and form, and that requires molecular-level solutions we've yet to fully develop."*

Dr. Marcus Nguyen
Chief of Advanced Wound Therapeutics at Johns Hopkins Medicine,
2023 Global Wound Care Summit

# Large, Growing US Market Allows For Massive Revenue Potential




## Rise in surgical procedures and diabetes leading to increase in surgical wound infections and DFUs:

### Rationale for targeting acute wounds initially:

1. Low cost, low risk, rapid clinical trial execution
2. Six Therapeutics initial data translates to this population
3. Massive revenue potential with conservative assumptions

### Massive revenue potential with conservative assumptions*:

| Share assumptions* | Projected annual revenues* |
|---|---|
| 1% | $350M |
| 5% | $2B |
| 10% | $3B |

The price assumption is $500/tube which is lower than comparable products

*This modelling is intended to illustrate the massive commercial potential with highly conservative share and price assumptions and targeting only acute wounds.

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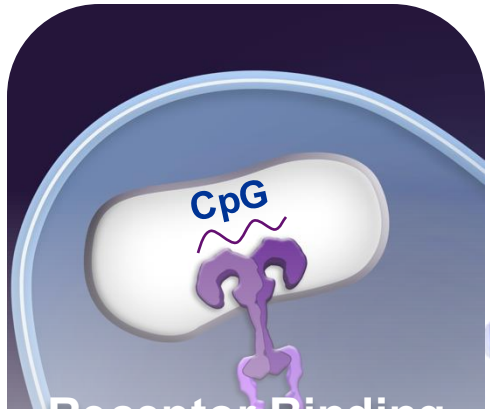
DFU = Diabetic foot ulcer

# Our Product Is A First-To-Market Topically Applied TLR9 Agonist

**Accelerated healing achieved by harnessing the immune system and stimulating a cellular response to injury:**

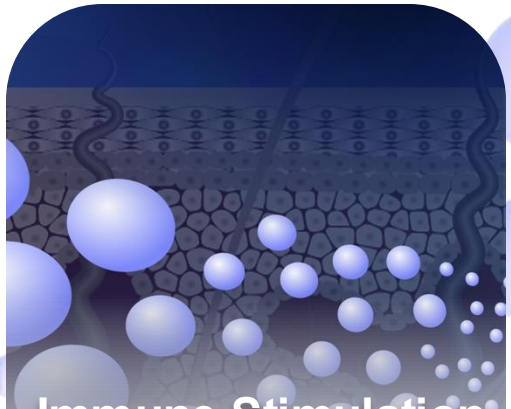

## Topical application

- Our product is a CpG, a synthetic, single-stranded DNA molecule
- Topical administration allows for ease of application and additional safety




## Receptor Binding

- CpG binds to the TLR9 receptor in the cell and stimulates the immune system (i.e. a TLR9 agonist)



## Immune Stimulation

- Pro-inflammatory and other substances released to accelerate healing

## Bioinspired Healing

**TLR9 agonists as a class have demonstrated proven long-term safety**

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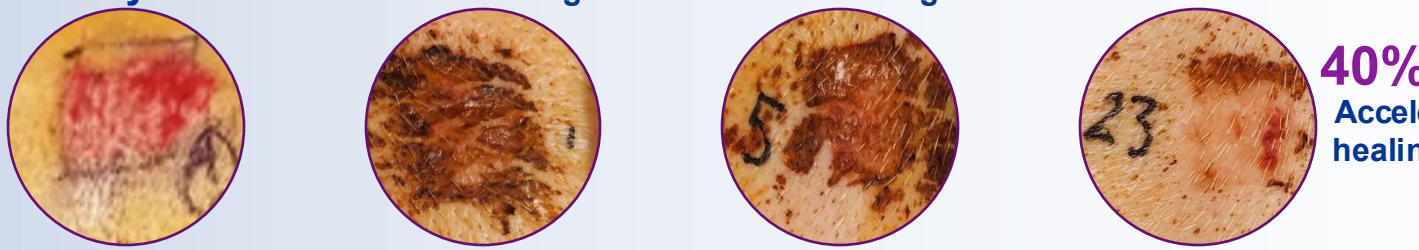
# Healing Data Demonstrated In Clinically Relevant Models Confirms Safety And Efficacy

## PIG MODEL

### PHOTOGRAPHIC EVIDENCE

**Assessment 1:**

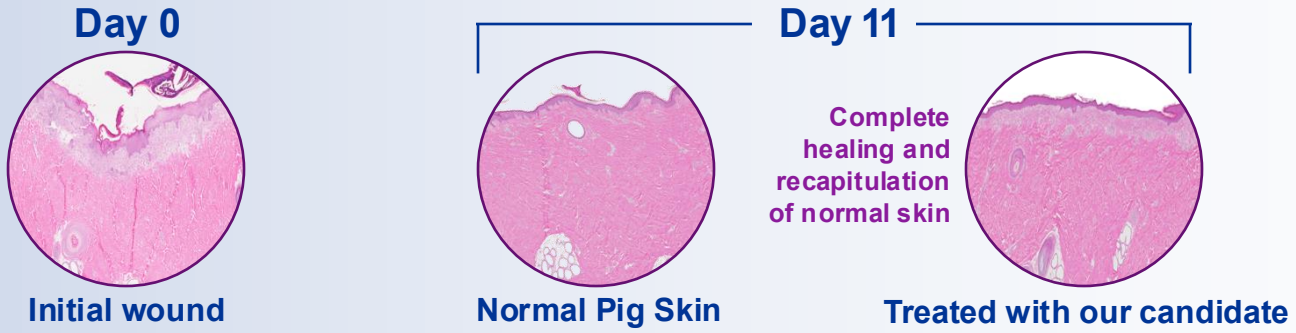
Photographic evidence of accelerated healing with Six Therapeutics candidate




### HISTOLOGICAL ANALYSIS

**Assessment 2:**

Histological analysis to demonstrate healing quality by comparing normal pig skin with skin healed with Six Therapeutics candidate



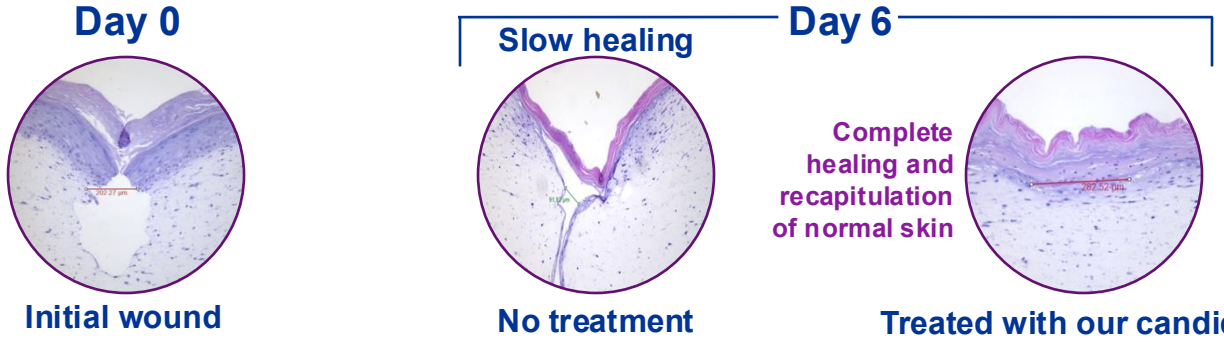

**Pig model study overview:**

- Pig data is required for IND approval by the FDA because it is very similar to human skin
- Data generated in partial thickness wounds
- Normal healing in this animal is 14 days
- Only three doses administered
- Topical application
- No clinical safety issues we observed

## HUMAN MODEL

### Human Living Skin Equivalent (HLSE) model:

Histological analysis to demonstrate speed and quality of healing with Six Therapeutics candidate




**Human Living Skin Equivalent (HLSE) model study overview:**

- Based on Labskin data (a HLSE), full-thickness, 3D human skin equivalent model that mimics the structure and function of human skin
- Normal healing for Labskin is 21 days
- Only three doses administered
- Topical application
- No local skin toxicity observed

# TLR9 Agonists Proven Safe Long-term In Multiple Applications And Methods Of Delivery

## FDA approved TLR9 agonists

As vaccine adjuvants

HEPLISAV-B®
Hepatitis B Vaccine (Recombinant), Adjuvanted

- Hepatitis-B vaccine developed by Dynavax Technologies
- Approved 2018

Cyfendus

- Anthrax vaccine developed by Emergent BioSolutions
- Approved 2023

## Ongoing Validation

As companies conduct human trials with TLR9 agonists

REGENERON
science to medicine®

TALLAC THERAPEUTICS

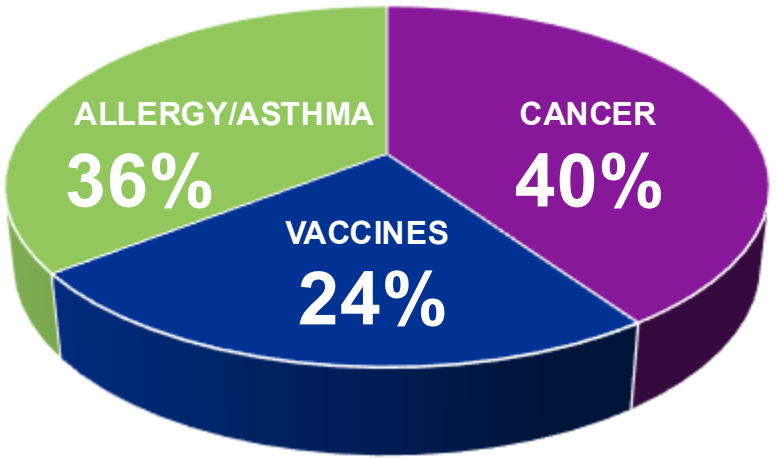
Bluejay THERAPEUTICS

elicio THERAPEUTICS

Luye GeneLeap

## Published data

Robust body of published data from human studies supporting TLR9 agonists




**No safety concerns in >12,000 patients and millions of doses administered**

# The Overall Path From Today To Commercial Approval Is Low-Cost, Straightforward And Derisked

Current ask: $3.5M to complete preclinical studies (see next slide)

## Fast path to market:

| | Development path to commercial approval: | | |
|---|---|---|---|
| **Milestones** | ★ IND Approval | | ★ NDA Approval |
| **Phase** | **Preclinical** | **Clinical** | **Total** |
| **Cost** | **$3.5M** | **$36.5M** | **$40M** |
| **Timing** | **1.5 years** | **3 years** | **5.5 years*** |
| **Derisking steps/ rationale** | • Validated MOA and class level safety demonstrated in >12,000 patients<br>• Six Therapeutics initial data demonstrates safety and efficacy in clinically relevant models<br>• Clearly defined FDA guidelines and proactive communications ensure alignment on regulatory strategy<br>• Large, uncomplicated pool of patients and short study durations expedite execution timelines<br>• Potential to run the clinical trials ex-US to further expedite timelines<br>• Veteran team to guide development and commercial launch | | |

* Includes NDA preparation and filing timeline

## Timely, cost-efficient clinical trial execution:

| | Phase I | Phase 2 | Phase 3 | Total |
|---|---|---|---|---|
| **Patient population** | Healthy volunteers | Surgical wounds | Surgical wounds | |
| **Study duration** | 120 days | 450 days | 545 days | 1,115 days (37 months, 3 years) |
| **Number of patients (n)** | 50 | 180 | 500 | 730 |
| **Cost per patient** | $50K | $50K | $50K | |
| **Total** | **$2.5M** | **$9M** | **$25M** | **$36.5M** |
| **Primary endpoint** | Statistical difference in time to wound closure versus placebo | | | |
| **Secondary endpoint** | Safety of TLR9 agonist versus placebo | | | |
| **Treatment period** | 14-28 days | | | |
| **Trial setting** | Outpatient clinics and/or patient's home | | | |

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# Seeking Capital to Achieve The Next Value Inflection Point

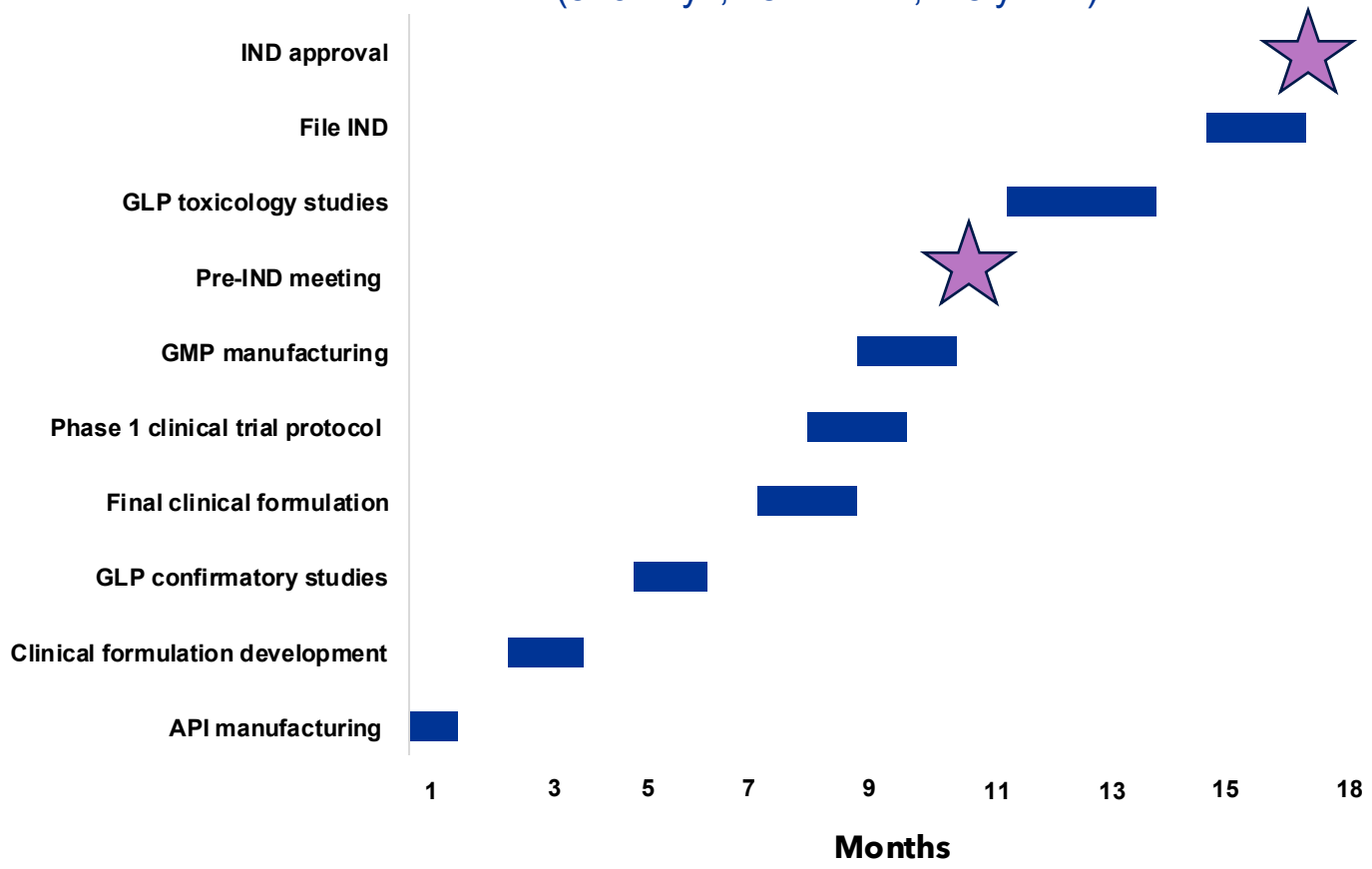
## Seeking $3.5M to advance development to IND approval within 1.5 years:

### Use of proceeds:

| Development activities to IND | | Budget |
|---|---|---|
| **Preclinical** | **$** | **1,650,000** |
| GLP toxicology studies | $ | 1,300,000 |
| GLP confirmatory studies | $ | 350,000 |
| **Manufacturing** | **$** | **540,000** |
| API manufacturing | $ | 65,000 |
| Clinical formulation development | $ | 180,000 |
| Final clinical formulation | $ | 75,000 |
| GMP manufacturing of clinical supplies | $ | 220,000 |
| **Regulatory** | **$** | **110,000** |
| File IND | $ | 30,000 |
| IND approval | | |
| Phase 1 clinical trial protocol | $ | 50,000 |
| Pre-IND meeting | $ | 30,000 |
| **Corporate** | **$** | **1,200,000** |
| Consultants, G&A | $ | 1,200,000 |
| **Grand Total** | **$** | **3,500,000** |

### Development path to IND approval

(540 days; 18 months; 1.5 years)




IND = Investigational New Drug; the approval by FDA to begin human clinical studies

= Regulatory milestone

# Proven Team with >100 Years Total Development and Commercial Experience

## LEADERSHIP

**Nyron Khan**
Co-founder & CEO
Commercial Lead
Led launches of several major Pharma brands at Roche, Alexion and Alcresta

**Howard L. Levine, Ph.D.**
Co-founder
CMC Lead
Proven thought-leader in biopharmaceutical product development and commercialization

**Dr. Simon Talbot**
Chair, SAB
Medical Lead
Plastic Surgeon at Mass General Brigham; Associate Professor of Surgery, Harvard Medical School

**Tom Biancardi, MBA**
Co-founder
Finance Lead
Experienced Finance leader with proven track record in fundraising and deal-making. Currently, CFO at Beacon Therapeutics.

**Prashant Girinath, Ph.D., J.D.**
Co-founder
Corporate Strategy Lead
Lifesciences attorney at Greenberg Traurig in Boston. Develops IP strategy and counsels on M&A.

## ADVISORS

**Dr. Ned Swanson**
Clinical Advisor
Co-founder, President and Chief Medical Officer of the wound healing company PolarityBio

**Dr. Anil Chandraker**
Scientific Advisor
(Immunology)
Professor and Chief of Renal Medicine at UMass Chan Medical School
Past President of the American Society of Transplantation

**Dr. Alice Bexon**
Scientific Advisor
(TLR9 Development)
CEO, Bexon Clinical Consulting.
Seasoned drug developer with specific expertise in helping early-stage companies.

**Shohreh Miller, DVM, PhD, DACLAM**
Scientific Advisor
(Preclinical Studies)
Director of In Vivo Services at Rutgers University. Deep expertise in translational science, preclinical development, and laboratory animal medicine.

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