



Investor Presentation

October 2020

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- **Post-operative pain treatment is a growing market (\$12B) with a need for better therapeutics¹**
 - Local anesthetics provide pain relief for up to 6 hours and require augmentation with NSAIDs or opioids for moderate to severe pain, leading to side effects and dependence
 - Opiate abuse and addiction cause 70,000 death in the US & an economic burden of \$80B/yr¹
 - Exparel (Pacira), the only known marketed long acting liposomal generic local anesthetic has >\$400M revenues: PCRX-market cap, at peak, over \$4.0B – an important benchmark for PainReform²
- **PainReform has developed PRF-110, a novel formulation extended release ropivacaine**
 - Robust **preclinical data package**
 - **Phase 1 data** in healthy volunteers suggest favorable PK profile and safety data
 - In a **Phase 2 study** clinical study in 15 open hernia patients PRF-110 demonstrated pain relief of up to 72 hours
 - **Phase 3 study design and IND approved; FDA confirmed 505(b)(2) designation**
 - Patent estate granted for PRF-110 and formulation platform through 2033 prior to extensions-for US, Canada, IL, Australian, Japanese, Russian and Chinese patents, other countries-pending
- **Clinical Development Plan**
 - Green light from **FDA to initiate two phase III trials** (soft and hard tissue) of ~400 patients each for NDA submission
 - 505(b)(2): A low risk barrier to approval

¹ White House [Report](#): Underestimated Cost of the Opioid Crisis

² Market Insider [Report](#): Pacira BioSciences Reports 2019 Results

1

**Innovative
Formulation /
Delivery System**

2

**Opioid Epidemic
Presents
Significant
Commercial
Opportunity**

3

**Seasoned
Management
Team with
Decades of
Experience**

4

**Robust US and
International
IP Portfolio**

5

**Core platform
can be utilized
for wide-range
of APIs to
generate
sustainable
pipeline**

Large Unmet Need in Non-Opioid Postoperative Pain Management¹

¹Market Watch Post-Operative Pain Management Market Size Analysis 2019 [Report](#)



Ehud Geller, PhD, MBA. Acting Chairman

- Former President & CEO of Interpharm Laboratories and EVP of Teva Group
- Former head of the Israeli Pharmaceutical Manufacturers Association and board member of the Tel Aviv Stock Exchange
- National Industry award for contribution to biotech industry and management leadership, Samuel Johnson Medal – Columbia
- Columbia University, Drexel Institute – Chemical Engineering (bio-chemical technology), MBA, PhD



Eli Hazum, PhD, MBA. Chief Technical Officer

- Spent 5 years at Glaxo Inc. as Head of Department of Receptor Research and Metabolic Diseases
- Over last 25 years Eli has taken leadership roles within Medica portfolio companies including interim CEO for Collgard Biopharmaceuticals and Ester Neurosciences, where he was responsible for executing Ester's acquisition by Amarin Pharmaceuticals.
- Received Ph.D. from the Weizmann Institute of Science in the field of hormone biochemistry, and has an executive MBA from Humberstone University in the UK



David E. Weinstein, MD, PhD. Chief Medical Officer and President

- Neurologist and Neuroscientist; former Professor in the Departments of Neuroscience, Neurology, Pathology and the Comprehensive Cancer Center at the Albert Einstein College of Medicine and Adjunct Associate Professor of Pathology, Columbia College of Physicians and Surgeons
- Seasoned biotech executive, with C-suite experience at InteKrin Therapeutics, GliaMed Therapeutics, RiverTown Therapeutics, Androbiosciences
- MS (Pharmacology), MD, and PhD from NYU and Columbia College of Physicians and Surgeons



Sigal Aviel, PhD, MBA. Chief Operating Officer

- Over 20 years of managerial experience in the Biotech industry.
- Prior to joining PainReform Sigal held the position of Chief R&D Officer at MediWound, a company specializing in deep burns and chronic wound care, where she was responsible for product development from early stages to final product approval by regulatory authorities.
- PhD in Immunology and Microbiology from Duke University Medical School as well as an executive MBA degree from the Kellogg school of business at NW University

Management Team



Ehud Geller, PhD, MBA. Acting Chairman



Eli Hazum, PhD, MBA. Chief Technical Officer



GlaxoSmithKline



Bio-Technology General



David E. Weinstein, MD, PhD. Chief Medical Officer



Albert Einstein College of Medicine



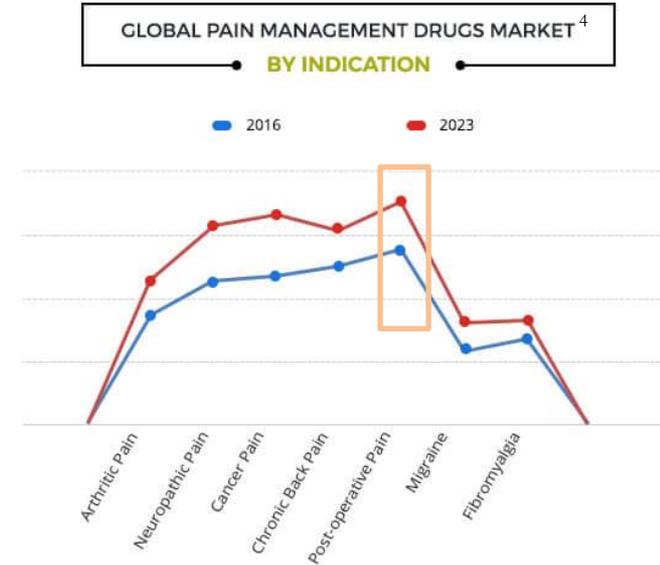
GliaMed, Inc.



Sigal Aviel, PhD, MBA. Chief Operating Officer



- The 2017 world-wide overall post-operative pain treatment market was estimated at US\$12B and is expected to reach in excess of US\$45B by the end of 2026¹
- Significant unmet need for long-acting local anesthetic agents in order to spare opioids use, their side effects and reduce hospital length of stay due to complications
- Over 40-45 million procedures in the US per year
 - Just 10% share provides >\$500M in US revenues²
- Despite the extensive use of opioids and NSAIDs, 76-86% of patients still experience moderate-to-extreme pain after surgery³
- Study of the global post-operative pain management market reveals a steady growth potential of **5.4% CAGR during the forecast period of 2017 to 2023**¹



POST-OPERATIVE PAIN segment holds a dominant position in 2016 and would continue to maintain the lead over the forecast period.

¹<https://www.persistencemarketresearch.com/market-research/postoperative-pain-management-market.asp>

²National Health Statistics Reports 2010 Surgery stats.pdf

³Gan, et al., Incidence, patient satisfaction, and perceptions of post-surgical pain: results from a US national survey. Curr Med Res Opin. 2014;30(1):149-160.

⁴Market Watch Post-Operative Pain Management Market Size Analysis 2019 [Report](#)



11.4 Million

People misused opioids in 2019. 886K used heroin. 562K misused both pain relievers and heroin³



2.1 Million

People have an opioid use disorder. 1.7 million people with a prescription pain reliever have a use disorder.³



62.6%

Of people listed pain as their main reason for opioid misuse where 36% of people with an opioid problem received a prescription from a healthcare provider³



>\$80.0 Billion

Per year US economic burden where 40,000 people a year die from opioid related issues²

- **99% of surgical patients** receive opioids to manage post-surgical pain¹
- Opioids dependency can start within **3 days** of initial use
- 6% to 10% of surgical patients discharged with opiate prescription develop an opioid-dependency⁵
- **75% of patients** who undergo surgery experience acute post-operative pain, which is often medium-high in severity⁴
- A 2016 study which enrolled 799,449 patients, showed that reliance on opioid analgesics as the mainstay for **perioperative pain management is still widespread.**³

¹ NSDUH, 2017 Data; published Sept. 2018

² Med Care 2016 54 (10) 901-906, [Article](#)

³ Hollmann: Optimal postoperative pain management – redefining the role for opioids [Study](#)

⁴ NIH Horn; Kramer – Postoperative Pain Control [Study](#)

⁵ Lee, et al Clin Oncol. 2017;35(36):4042–9.



Short Acting Opioids

- Repeated dosing required
- Inconsistent pain control between doses
- Dependence risk increases with treatment duration
- Significant adverse effects

Long Acting Opioids

- Poor efficacy in acute pain control
- Not intended for the treatment of post-operative pain
- Significant adverse effects

Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

- Moderate efficacy in acute pain control
- Repeated dosing required
- Inconsistent pain control between doses
- Significant safety issues, including bleeding, stroke, gastritis, renal toxicity



Extended release, Local, Non-Opioid Analgesic (Exparel®)

- Limited efficacy in acute pain control
- Liposomal bupivacaine
- Reduced postoperative opioid use
- Approved - revenues \$400M
- Complex production-price
- Handling/delivery limitations



Pain Reduction Time

Studies have shown 48 hours of pain reduction in healthy volunteers and about 72 hours in a clinical setting



Scalable and Cost Effective

Low variable costs allows for ease of manufacturing and production to meet high market demand



Easy Application

Avoiding multiple injection reduces delivery time and complexity, reduces the risk of hematoma

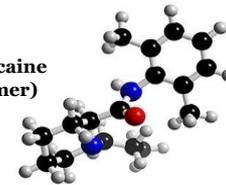


Core Platform

Platform can be utilized for a wide-range of APIs to generate sustainable pipeline of new product applications

- PainReform has developed a platform formulation for extended release of drugs
- Low COGS compared to current drug landscape¹
- Reliable PK and low Cmax
- No free API
- Physical attributes provide ease of surgeon use
- No injections, thereby avoiding risk of inadvertent systemic administration
- Robust IP portfolio

Ropivacaine
(s-isomer)

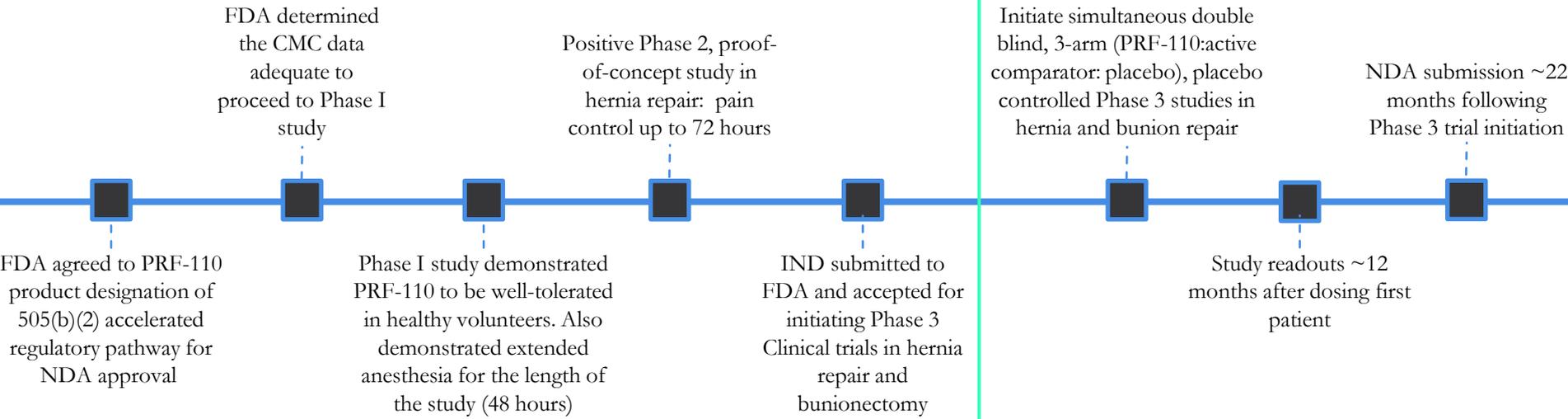


¹ <http://investor.pacira.com/static-files/45381cc5-0e49-4eb1-9263-939ea396a716>

PRF-110: Timeline to NDA

Historical

Future (post Funding)



Source: <http://www.goldmansachs.com/our-thinking/pages/music-in-the-air.html>

Product differentiation PRF-110 vs. Competition



	Pacira ¹ – Exparel™	Heron ² -HTX 011	PRF-110	PRF-110 Advantages
Formulation	Watery, complex liposomal suspension	Biochronomer technology ⁽⁴⁾ : Non-dilutable (Limited market)	Waterless, viscous, oil-based solution (GRAS)	Uniformity, viscosity, & retention
Pain intensity reduction time	12-24 hours in surgical setting. Not significantly better than Bupivacaine alone	Pain control up to 72 hours. Nerve block-problematic. AEs: Site inflammation, necrosis, bradycardia and impaired wound healing (Pacira citizen petition)	Approx. 72 hours pain control in clinical setting	Potentially longer duration of clinical activity, well-tolerated, no injection-related inflammation, infection or accidental systemic exposure
Manufacturing & Market	Special equipment & complex methodology resulting in high COGS; US only	Complex chemistry and methodology	Simple, short standard process and formulation, leads to \$5-10/u; WW	Scalable and cost effective, WW market
Status	Product launched in 2012, sales \$400M in 2019	Completed phase III; petition by Pacira. CRL from the FDA (3/4/19) requesting additional CMC and pre-clinical information	Preparing for Phase III, expected launch in 2022	
Valuation³	\$2.6 Billion	\$1.4 Billion		

¹ Pacira published data, news, presentation

² Heron published data, news, presentation

³ As of 8/14/2020

⁴ The Biochronomer® polymer is a semi-solid, highly viscous polyorthoester polymer & alpha-hydroxy (e.g., lactic & glycolic) acids are incorporated into the polymer backbone to promote degradation. Hydrolysis releases drugs while creating acidic environment.

- PainReform carried out extensive FDA requested wound healing and related animal studies that showed:
 - ✓ PRF-110 **allows for normal wound healing of surgical incisions** equal to both Naropin® and saline without any untoward histological or radiologic (microCT) effects observed in soft or bony tissue
 - ✓ Tensile strength of healed surgical skin following exposure to PRF-110 is equal to that of incisions exposed to either Naropin® or saline
 - ✓ Integrity of surgical sutures and surgical meshes is not affected by PRF-110 (compared to saline)
 - ✓ **No systemic side effects** observed in any models
- PRF-110 safety in human trials showed **no systemic, wound healing or scarring abnormalities**. Wound healing in all patients was complete and similar to that expected in surgery without PRF-110

- **Efficacy**

- PRF-110 provided post-operative pain control for up to 72 hours after a single application

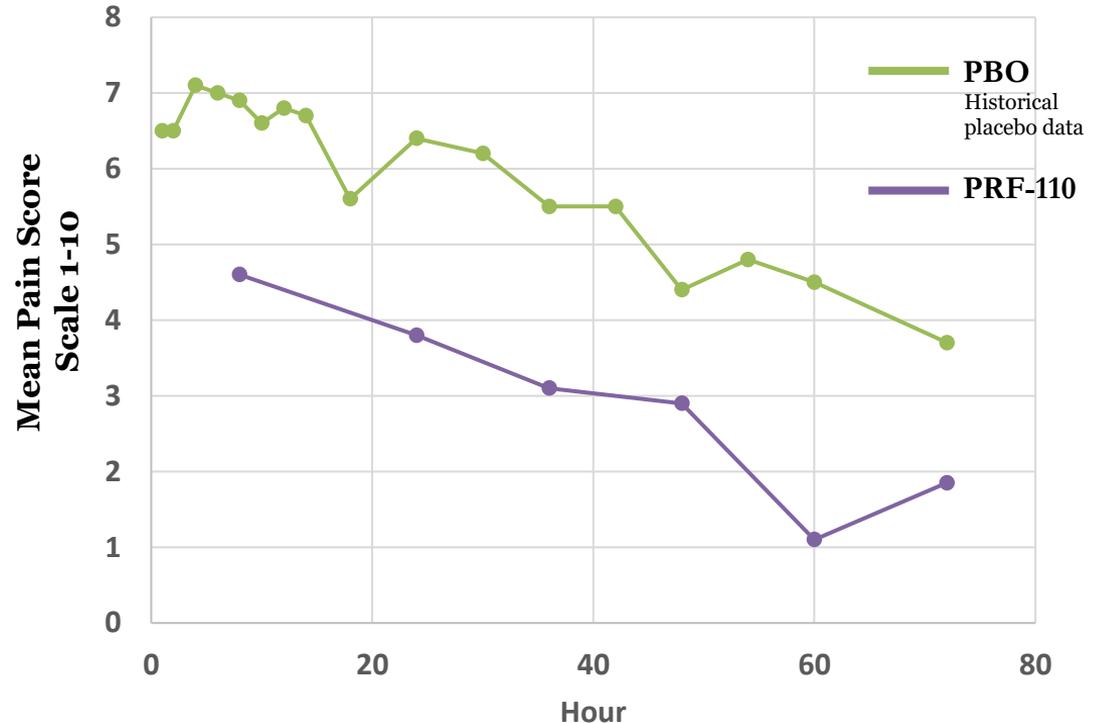
- **Safety**

- PRF-110 was well tolerated

- **Ease of use**

- easy to use and compliant with standard surgical techniques

PRF-110 Pain Reduction Up to 72-Hours After a Single Application



- **Two, double blind, placebo control 72-hour treatment period**, studies planned (bunionectomy and hernia repair). For each study:
 - Three cohorts (n= ~400): 1. PRF-110; 2. Naropin[®] (ropivacaine); placebo; in a 2:2:1 ratio
 - Primary endpoint (Efficacy)
 - Mean pain scores over 72 hours (scale 1-10), compared to placebo
 - Secondary endpoints (Safety)
 - Incidence of TEAEs and Serious AEs (SAEs)
 - Physical examination
 - Wound Healing
 - Secondary endpoints (Efficacy)
 - Mean pain scores over 72 hours (scale 1-10), compared to placebo
 - Proportion of subjects who are opioid-free for PRF110 compared with active comparator Naropin[®] over 72 hours



Efficacy

Cross study comparison of Phase II data, 72 hours pain AUC



Safety

Met FDA required extensive pre-clinical studies to demonstrate no wound healing issues



Administration

PRF-110 viscosity and uniformity are highly suitable for standard surgical site administration.



COGS

Low cost of good sold allows a highly strategic pricing plan and considerations



Large Unmet Need in Non-Opioid Postoperative Pain Management¹

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The logo for PainReform features the word "PainReform" in a serif font. The word "Pain" is colored green, and "Reform" is colored blue. A blue swoosh underline starts under the "P", loops around the "R", and ends under the "m".

PainReform

A solid blue horizontal banner with the text "Thank You" centered in a white serif font. The banner is flanked by thin green lines above and below it.

Thank You