



CORPORATE PRESENTATION
NOVEMBER 2021



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PolyPid Overview

PolyPid is a Phase 3 clinical-stage biopharmaceutical company focused on developing targeted, locally administered and prolonged release therapeutics to address diseases with high unmet medical needs

Polymer-Lipid Encapsulation matrix (PLEX) Platform

Our proprietary matrix of several thousand layers of polymers and lipids that physically embed an active drug and enable a customizable, predetermined release rate of up to several months

Lead Product

D-PLEX₁₀₀ is currently in Phase 3 development for the prevention of surgical site infections (SSIs) following abdominal (soft tissue) or post-cardiac sternal (bone) surgeries

101

issued patents⁽¹⁾



>80

employees⁽¹⁾

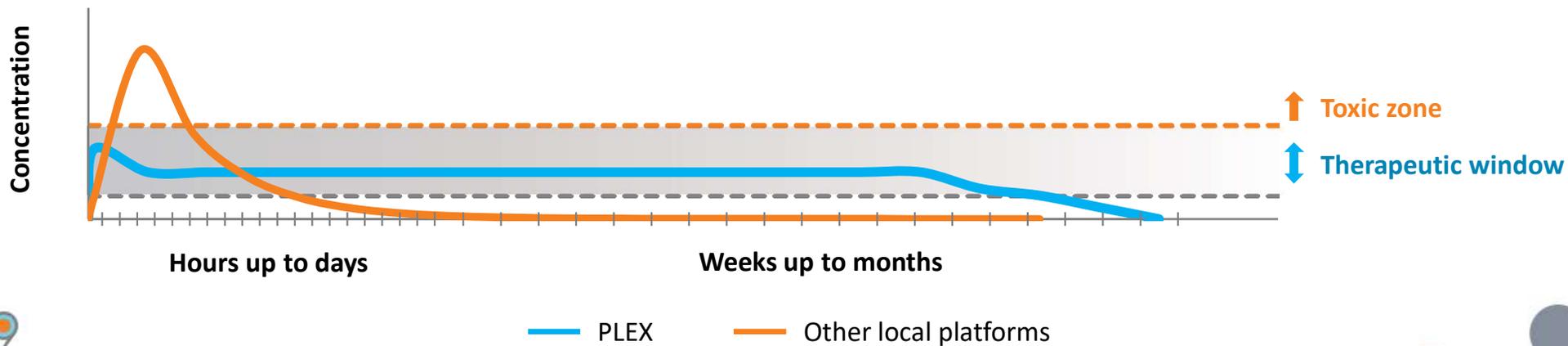
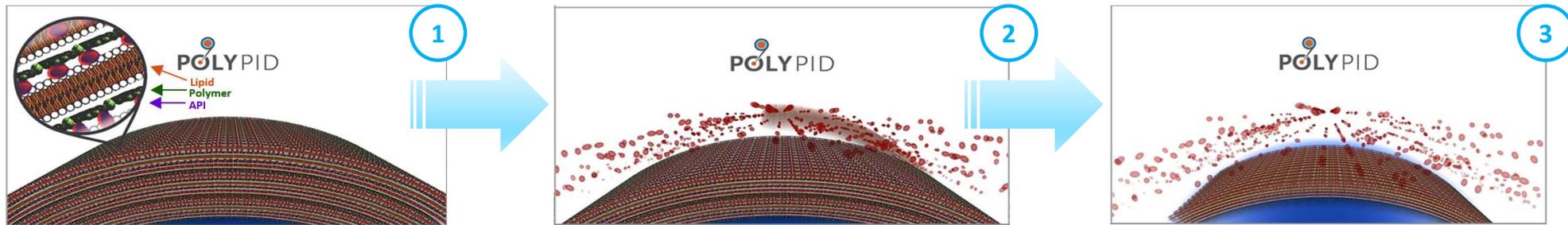


HQs

Global: Petach Tikva, Israel
US: Summit, NJ



D-PLEX₁₀₀ – Localized Drug Delivery System that is Optimized for the Management of Surgical Site Infections (SSIs)



D-PLEX₁₀₀ - Localized Drug Delivery System Optimized for Prevention of SSIs

✓ **Active Ingredient:**
Doxycycline
(broad spectrum antibiotic)

✓ **Release Duration:**
Prolonged effect up
to 4 weeks

✓ **Indication:** prevention of post
cardiac surgery sternal infection
and post abdominal surgery
incisional infection

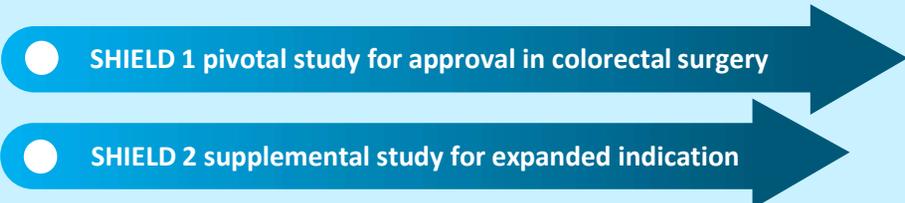
✓ **Release profile:**
Constant & linear release

✓ **Dosing:** Varies by incision size.
1 vial < 10cm,
10cm < 2vials < 20cm, 3 vials >20cm

✓ **Effective release rate:**
To overcome resistant
bacteria & biofilm



Pipeline Summary

Product candidate and indication	Preclinical	Phase 1	Phase 2	Phase 3	Key milestones
 <p>D-PLEX₁₀₀ Prevention of SSI in soft tissue (abdominal)</p>	 <ul style="list-style-type: none"> SHIELD 1 pivotal study for approval in colorectal surgery SHIELD 2 supplemental study for expanded indication 				<ul style="list-style-type: none"> SHIELD 1 approval sufficient for FDA approval First patient enrolled in July 2020 Top-line results expected by Q3 2022
 <p>D-PLEX₁₀₀ Prevention of SSI in bone tissue (sternum)</p>					<ul style="list-style-type: none"> First patient enrolled in Feb. 2020
 <p>OncoPLEX Intratumoral therapy</p>					<ul style="list-style-type: none"> Pre-clinical stage

Unencumbered, late-stage pipeline with near-term value inflection

The Burden of Surgical Site Infections

Up to 30%

Estimated SSI rate of patients undergoing colorectal surgery^{1,2}



7-11 days

Additional post-operative hospital days for patients with SSIs³



20%

SSI rate of all health care-associated infections in US hospitals³



2-11x

Increased risk of death for SSI patient (up to 40% mortality after deep sternal infection)¹



\$11k-26k

Cost of treatment per infection directly attributable to SSIs



US **\$10bn** EU **~€11bn**

Estimated SSI-related incremental annual hospital costs in the US and EU^{4, 5}



¹ Deverick J et al, Strategies to Prevent Surgical Site Infections in Acute Care Hospitals: 2014 Update, Infection Control and Hospital Epidemiology, 2014. ² Estimated figures likely underestimated as ~50% of SSIs become evident only after a patient has been discharged. ³ The Joint Commission for Transforming Healthcare <https://www.centerfortransforminghealthcare.org/improvement-topics/surgical-site-infections/>. ⁴ Surgical site infection - a European perspective of incidence and economic burden. Leaper DJ et al. Int Wound J. 2004 Dec;1(4):247-73. ⁵ ~€11bn represents the midpoint of the range discussed in WHO Global guidelines on the prevention of surgical site infection. Nov 2016: 29; ⁶ New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Benedetta Allegranzi et al. Lancet Infect Dis. 2016 Dec;16(12):e288-e303. ⁷ Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, JAMA Surgery, Special Communication, 2017



A Globally Recognized Problem

SSI GUIDELINES:



What's New and What's Not

“The human and financial costs of treating surgical site infections (SSIs) are increasing. The number of surgical procedures performed in the United States continues to rise, and surgical patients are initially seen with increasingly complex comorbidities.”⁷

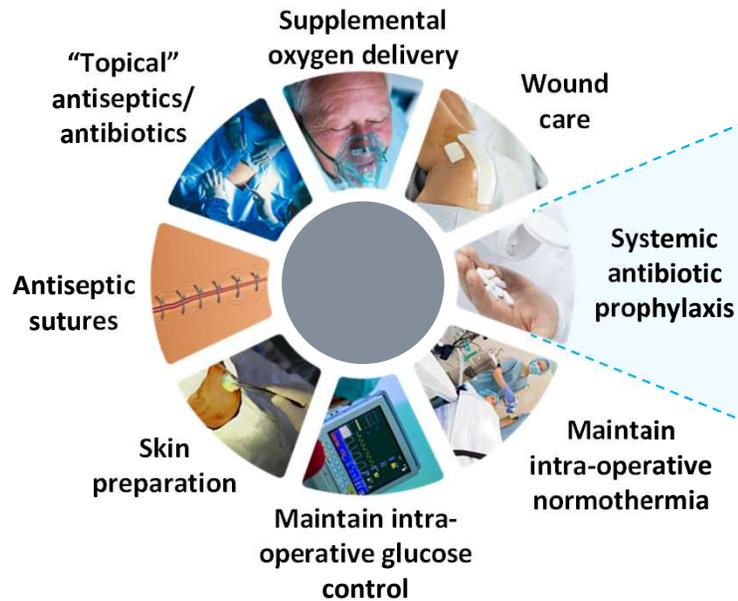


World Health Organization

“The prevention of SSIs is complex and requires the integration of a range of preventive measures before, during, and after surgery. No international guidelines are available...the prevention of SSIs is a priority for patient safety.”⁶

Our Initial Focus: Enhancing Post-Operative SSI Prevention

The Current Paradigm



Systemic Antibiotics Are Not Enough

- Systemic antibiotic prophylaxis (IV, Oral) ½ - 1-hour before the surgery is generally used to prevent SSIs
- Antibiotic penetration to the surgical wound is significantly limited due to the blood flow interruption cause by the incision^{1,2*}

In SSIs, the surgical incision becomes contaminated by bacteria



Our solution:
Direct local
antibiotic
administration
 at
 the site

Selected Key Players

Medtronic
 TYRX Absorbable
 Antibacterial Envelope

Johnson & Johnson
 ▶ **ETHICON**

Smith+Nephew
 PICO[®] 7

3M
 Acelyty[™]
 prevena

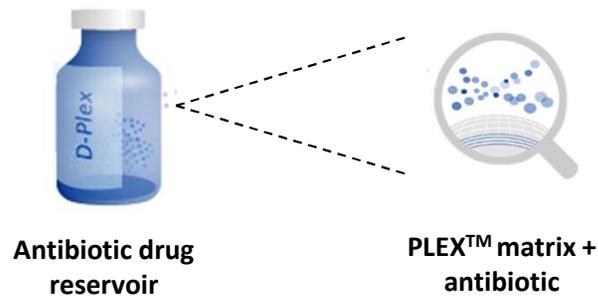
POLYPID

The Goal: effective and safe antibiotic concentrations over prolonged period within the surgical site

Source: American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. Ban et al. J Am CollSurg Vol. 224, No. 1, January 2017; New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective - Benedetta Allegranzi et al. The Lancet Infectious Diseases, Vol. 16, No. 12*In CABG, left internal mammary artery (LIMA) harvesting further decrease antibiotic penetration; Furthermore, Tissue perfusion is impaired in patients with diabetes or atherosclerosis, who are common in CABG / cardiac Surgery. 1 Cefazolin and linezolid penetration into sternal cancellous bone during coronary artery bypass grafting. Martin Andreas et al. European Journal of Cardio-Thoracic Surgery 48 (2015) 758-764; 2 Direct sternal administration of Vancomycin and Gentamicin during closure prevents wound infection. Andreas M. et al. Interactive CardioVascular and Thoracic Surgery (2017) 1-5.

D-PLEX₁₀₀ is a potential game changer in the prevention of SSIs

- PLEX technology used to physically encapsulate a broad spectrum antibiotic
- Designed to provide localized and prolonged infection management after surgery



Example of surgeon spreading the D-PLEX₁₀₀ paste in an open-heart surgery

D-PLEX₁₀₀: locally-administered doxycycline

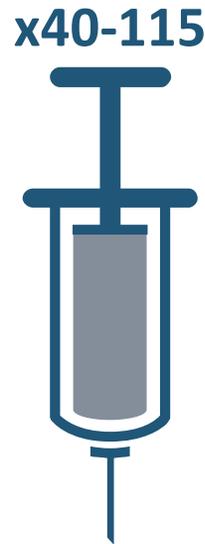
- Administered **directly in the surgical site**
- Local constant, effective concentration of antibiotic over **prolonged duration** (4 weeks)
- **Simple administration** that requires no additional training

A Small Single Dose of D-PLEX₁₀₀ is Sufficient for High Local Concentrations for Several Weeks

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Local delivery
of doxycycline

55-164 mg



Systemic formulation
of doxycycline

60 pills = 6,000 mg



D-PLEX₁₀₀ is designed to provide prolonged delivery following single administration and subsequent high local concentrations and has the potential to supersede existing antibiotic delivery systems, and may offer advantages over systemic treatments in the prevention of SSIs, including against many antibiotic-resistant bacterial strains

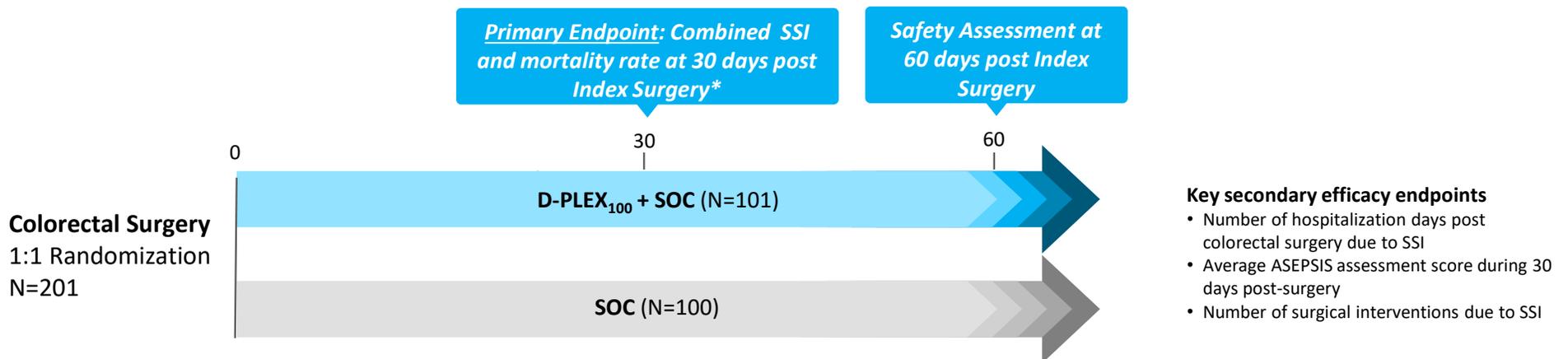
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Phase 2: D-PLEX₁₀₀ for the Prevention of Post Abdominal Surgery (Soft Tissue) SSIs



Assess efficacy and safety of D-PLEX₁₀₀ for prevention of deep and incisional SSI after elective abdominal colon surgery

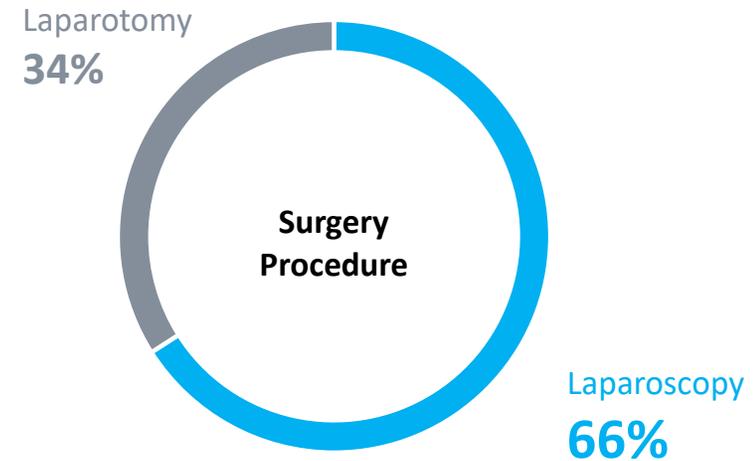
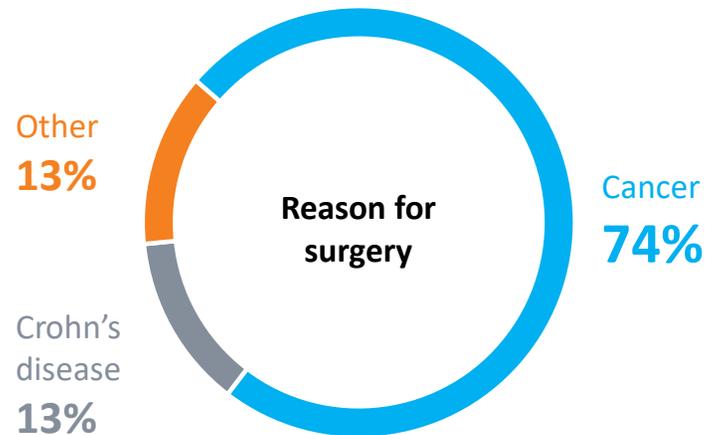
(prospective, multicenter, randomized, controlled, two arm study)





Demographics and Baseline Data Summary Statistics

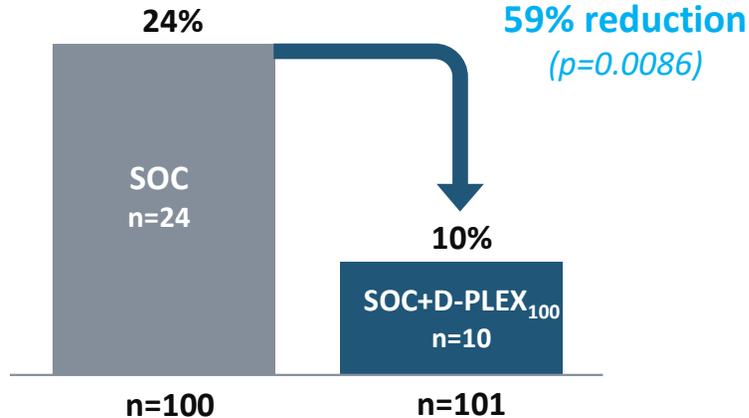
Baseline demographic (Age, BMI etc) and surgical characteristics were balanced between the two treatment groups



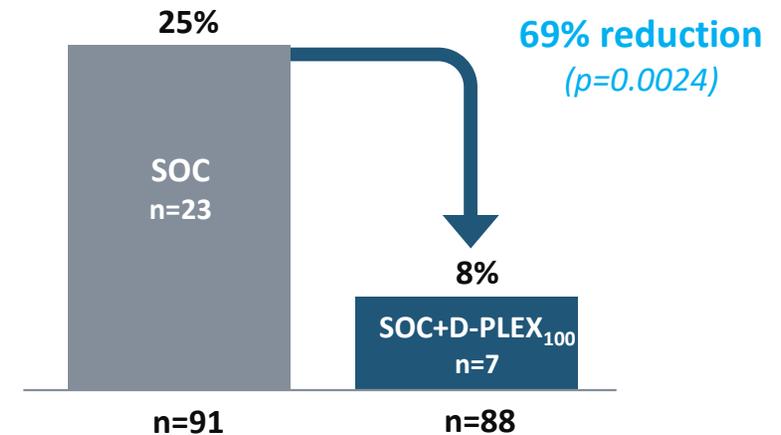


Positive Phase 2 Results in Abdominal Surgery

Primary Endpoint* ITT Analysis



Primary Endpoint - Per Protocol Analysis

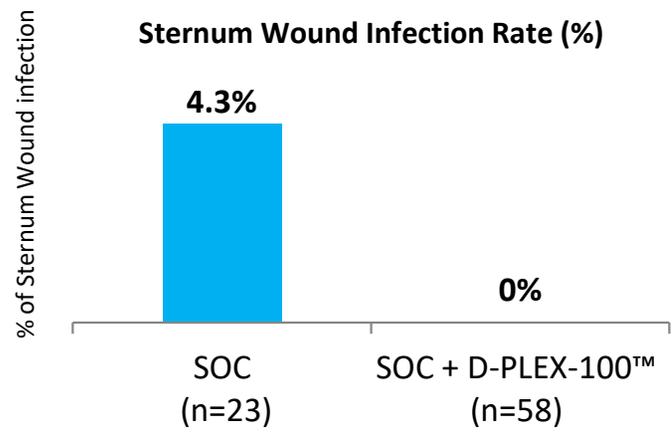


- 5 deaths observed in the SoC treatment arm, as compared to zero observed in the D-PLEX₁₀₀+SOC treatment arm within the first 60 days post-surgery ($p=0.0290$)
- Generally well tolerated, with no confirmed drug-related SAEs and no increase in wound healing impairment at the incision site as compared to control



D-PLEX in Sternal / Bone Surgeries

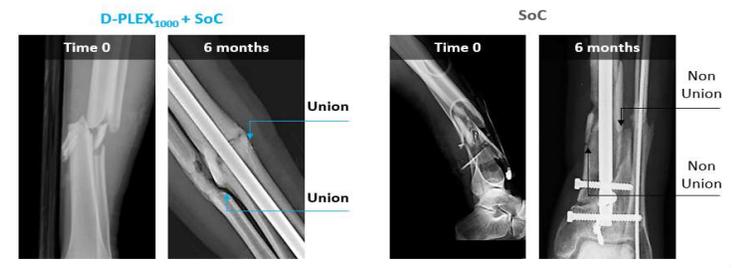
D-PLEX₁₀₀: P1b / 2 Open Heart Surgery Results¹



No Sternal Wound Infection in 58 Treated patients
 (Based on recent literature, we would have expected ~3-5 patients with SWIs in the D-PLEX₁₀₀ treatment group and 1-2 patients in the SoC control group)⁶⁻¹⁰

D-PLEX₁₀₀₀: Open-Tibia Fractures¹¹

	D-PLEX ₁₀₀₀ + SoC	SoC
Deep bone infections ² / non-union ³ rate (%)	0% (0/24)	11.1% (3/27)



No deep bone infections after 6 months across 24 treated patients, in comparison with reported incidences in the literature ranging between 7% to 19%⁴⁻⁵

No treatment related SAEs



¹ Modified ITT results, based on 3 months follow-up Clinical Study Report; ² One event; ³ Two events where another surgery and implantation of bone graft was needed; ⁴ Prodromidis et al. The 6-Hour Rule for Surgical Debridement of Open Tibial Fractures: A Systematic Review and Meta-Analysis of Infection and Nonunion Rates. 2016; ⁵ Poletti FL et al. Current Concepts and Principles in Open Tibial Fractures - Part II Management and Controversies. 2017. ⁶ Adding vancomycin to perioperative prophylaxis decreases deep sternal wound infections in high-risk cardiac surgery patients. Reneike S. et al. European Journal of Cardio-Thoracic Surgery (2017) 1-7 ⁷ Direct sternal administration of Vancomycin and Gentamicin during closure prevents wound infection. Andreas M. et al. Interactive CardioVascular and Thoracic Surgery (2017) 1-5 ⁸ Prevention of surgical site sternal infections in cardiac surgery: a two-centre prospective randomized controlled study. Schimmer C et al. European Journal of Cardio-Thoracic Surgery (2016) 1-6. ⁹ Based on 3 months follow-up interim report. ¹⁰ Surgical Site Infections Volume-Outcome Relationship and Year-to-Year Stability of Performance Rankings. Calderwood MS. et al. Med Care 2017;55: 79-85; ¹¹ Predecessor product candidate to D-PLEX100.

5 Trials Completed and Two Potentially Pivotal Phase 3 Trial Underway

D-PLEX has already completed 5 clinical trials with c. 400 patient data set





Recognizes the Potential Value of DPLEX₁₀₀ in SSI



2 Fast Track Designations

- More **frequent meetings** with the FDA to discuss the development plan
- Eligible for accelerated approval and priority review, if relevant criteria are met
- **Rolling Review**



2 Qualified Infectious Disease Product (QIDP) Designations

- All the benefits of Fast Track
- Additional **5-years of market exclusivity**
- **Improved CMS add-on payment**, increase of the NTAP from 50% to 75%



Breakthrough Therapy Designation

- All the benefits of Fast Track
- Intensive **guidance from FDA** on an efficient drug development program
- Organizational **commitment from FDA** involving senior managers

D-PLEX₁₀₀ Could Provide Clinical Benefit in Broad Surgical Population



Soft Tissues

General Surgeries

- Open Abdominal/GI/Colorectal Surgeries
 - Stomach & Intestinal
 - Herniorrhaphies
 - Colorectal
 - Cholecystectomies
 - Appendectomies

Selected Gynecological / Urological Surgeries

Hysterectomies ; Salpingo-Oophorectomies & Oophorectomies ;
Breast Reconstruction ; Prostatectomies ; Nephrectomies



Bone Tissues

Cardiac

- Open-Heart Surgeries (CABG, valve repair / replacement, heart / lung transplant, congenital defect repair)

Orthopedic

- Fractures
- Hip Arthroplasties (primary + Revision)
- Knee Arthroplasties (primary + Revision)
- Spine Fusions (Cervical, Thoracic and Lumbar)

US market represents c.14M major surgeries ¹

Key CMS Programs are Strong Drivers for D-PLEX₁₀₀

HAC reduction

Hospital-Acquired Condition Reduction

- CMS's non-payment for HACs - SSIs
- Total Medicare payments to facilities reduced by 1%
- Payment adjusted on all CMS claims
- Public reporting of quality measures

HRRP

Hospital Readmissions Reduction

- Incentivize hospitals to decrease readmission rates (frequently are caused by HAIs)
- Payment reductions are applied (up to 3% of all Medicare base operating DRG payments)

VBP

Value-Based Purchasing

- CMS rewards acute-care hospitals with incentive or penalties for the quality of care they provide (up to 2% of DRG payment)
- Episodes of care for 90 days

In 2019, Medicare penalized 7 of the 21 hospitals on the U.S. News Best Hospitals Honor Roll¹



Hospital	HAC penalty ²	Readmission penalty ²
UPMC Shadyside in Pittsburgh	\$2,720,780	\$977,439
Ronald Reagan UCLA Medical Center in L.A.	\$2,400,390	\$347,034
Keck Hospital of USC	\$1,553,190	\$92,152
Stanford Health Care's main hospital in Northern California	\$3,704,170	\$88,052
UCSF Medical Center in San Francisco	\$3,388,430	\$397,376
NewYork-Presbyterian/Weill Cornell Medical Center in Manhattan	\$7,441,260	\$1,677,600
Mayo Clinic's hospital in Phoenix	\$1,787,440	\$233,798

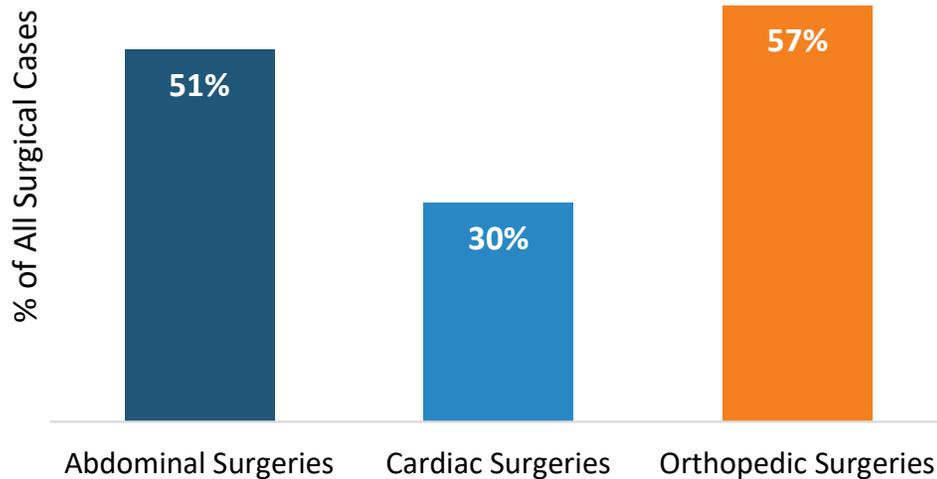
In fiscal 2020, CMS will withhold an estimated \$563 million in Medicare payments to hospitals under the Hospital Readmissions Reduction Program³

Surgeons and non-surgeons anticipate high adoption rate of D-PLEX₁₀₀

Anticipated Use of D-Plex₁₀₀ By Surgery and Respondent Type

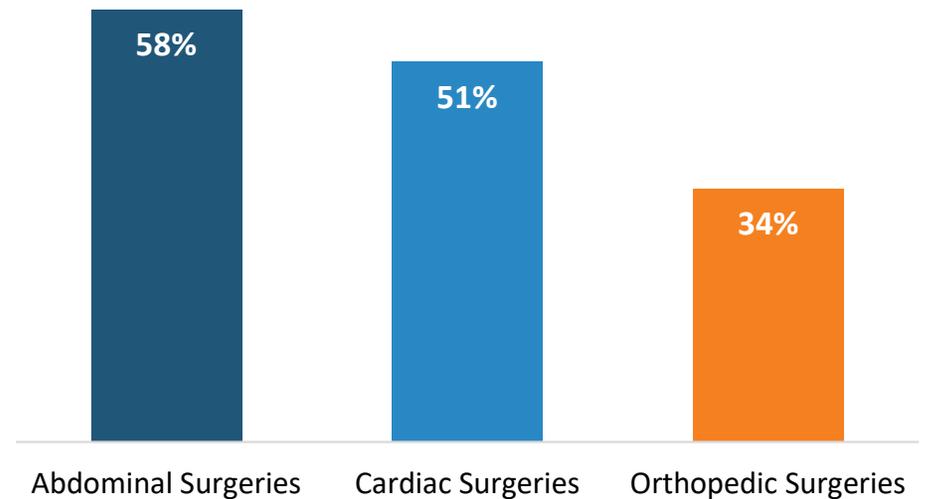
Surgeons

Abdominal n=17; Cardiac n=10; Orthopedic n=10



Non-Surgeons

n=34* (IDs n=7; Admins n=27)



Feedback from the market research study



*"The fact that you leave it in there for 28 days, that's interesting...because a lot of our **wounds get infected way down the road.**" –Cardiac Surgeon*



*"If there's a sustained release over a period of weeks, that would continue antibiotic presence in a wound that is trying to heal with open incision. This **keeps the fires burning in terms of antibiotic presence.**" –Infectious Disease Specialist*



*"Any infection needs to be reported. If there's a readmission for infection and that procedure was performed at the hospital, that **case is reviewed by Head of Orthopedics and the Infectious Disease Specialist.**" – Orthopedic Surgeon*



*"I think if Product X caused a 69% reduction in surgical site infection, I think **anybody who wouldn't use it would be doing a detriment to the patient, if the contrast is so stark.**"
– Colorectal/Abdominal Surgeon*

State-of-the-Art Manufacturing Facility



PolyPid was granted Manufacturer Authorization and Good Manufacturing Practice (GMP) certification by Israel's Ministry of Health (IMOH) and EU qualified person for its state-of-the-art ~10,500 square feet GMP manufacturing facility



- Investment – machinery, qualifications and validations
- Supply capacity – meets commercial demand for at least 30 months from launch

Summary

POLYPID is poised
for potential near-
term value creation



- Pursuing expedited development pathway
- Large and growing target market
- Broad applicability of PLEX technology
- Near-term value inflection points
- Strong management team