



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-PLEX<sub>100</sub> 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<sup>(1)</sup>



**>80**

employees<sup>(1)</sup>

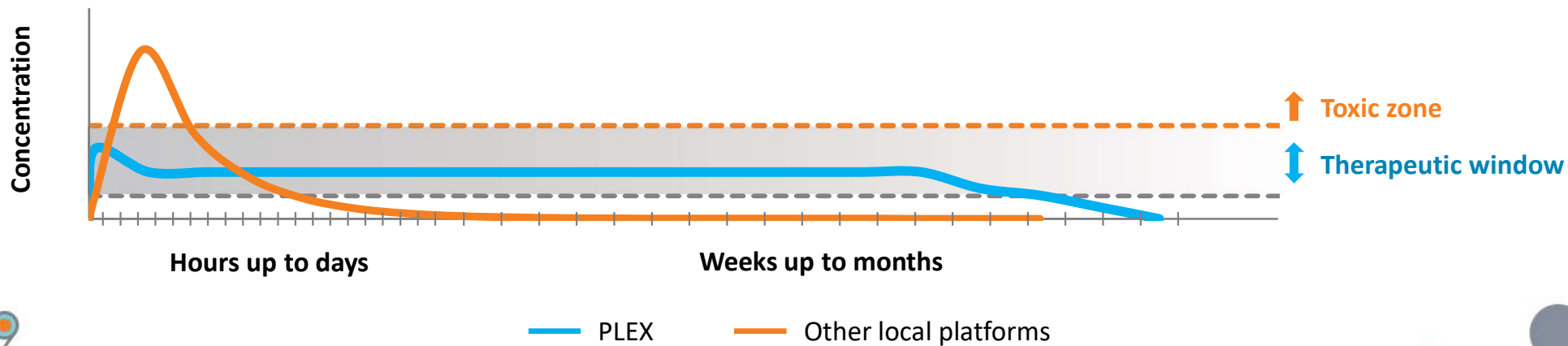
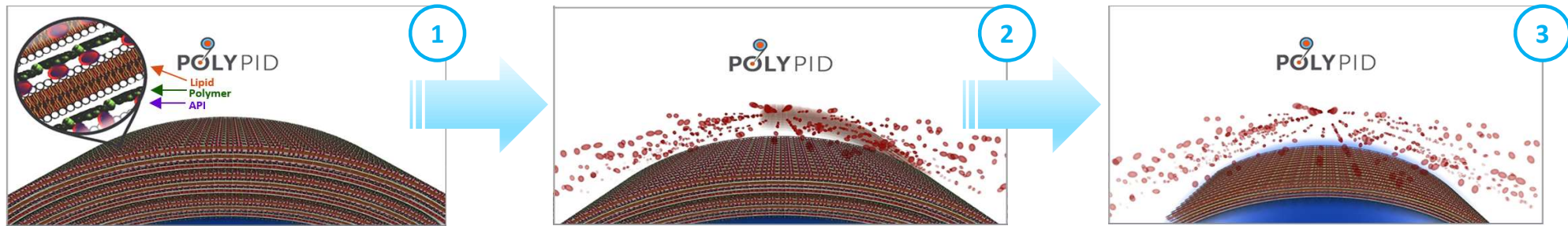


**HQs**

**Global:** Petach Tikva, Israel  
**US:** Summit, NJ



# D-PLEX<sub>100</sub> – Localized Drug Delivery System that is Optimized for the Management of Surgical Site Infections (SSIs)



## D-PLEX<sub>100</sub> - Localized Drug Delivery System Optimized for Prevention of SSIs

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

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

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

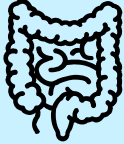
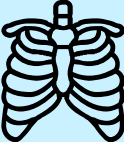

✓ **Release Duration:**  
Prolonged effect up to 4 weeks

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

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



## Pipeline Summary

Product candidate and indication		Preclinical	Phase 1	Phase 2	Phase 3	Key milestones
	<b>D-PLEX<sub>100</sub></b> Prevention of SSI in soft tissue (abdominal)	<div> <div></div> <div>SHIELD 1 pivotal study for approval in colorectal surgery</div> </div> <div> <div></div> <div>SHIELD 2 supplemental study for expanded indication</div> </div>				<ul style="list-style-type: none"> <li>SHIELD 1 approval sufficient for FDA approval</li> <li>First patient enrolled in July 2020</li> <li>Top-line results expected by Q3 2022</li> </ul>
	<b>D-PLEX<sub>100</sub></b> Prevention of SSI in bone tissue (sternum)	<div> <div></div> </div>				<ul style="list-style-type: none"> <li>First patient enrolled in Feb. 2020</li> </ul>
	<b>OncoPLEX</b> Intratumoral therapy	<div> <div></div> </div>				<ul style="list-style-type: none"> <li>Pre-clinical stage</li> </ul>

*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<sup>1,2</sup>



**7-11 days**

Additional post-operative hospital days for patients with SSIs<sup>3</sup>



**20%**

SSI rate of all health care-associated infections in US hospitals<sup>3</sup>



**2-11x**

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



**\$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<sup>4, 5</sup>



**POLYPID**

<sup>1</sup> Deverick J et al, Strategies to Prevent Surgical Site Infections in Acute Care Hospitals: 2014 Update, Infection Control and Hospital Epidemiology, 2014. <sup>2</sup> Estimated figures likely underestimated as ~50% of SSIs become evident only after a patient has been discharged. <sup>3</sup> The Joint Commission for Transforming Healthcare <https://www.centerfortransforminghealthcare.org/improvement-topics/surgical-site-infections/>; "Surgical site infection - a European perspective of incidence and economic burden. Leaper DJ et al. Int Wound J. 2004 Dec;1(4):247-73. <sup>4</sup> ~€11bn represents the midpoint of the range discussed in WHO Global guidelines on the prevention of surgical site infection. Nov 2016: 29; <sup>5</sup> 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. <sup>6</sup> 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."**<sup>7</sup>

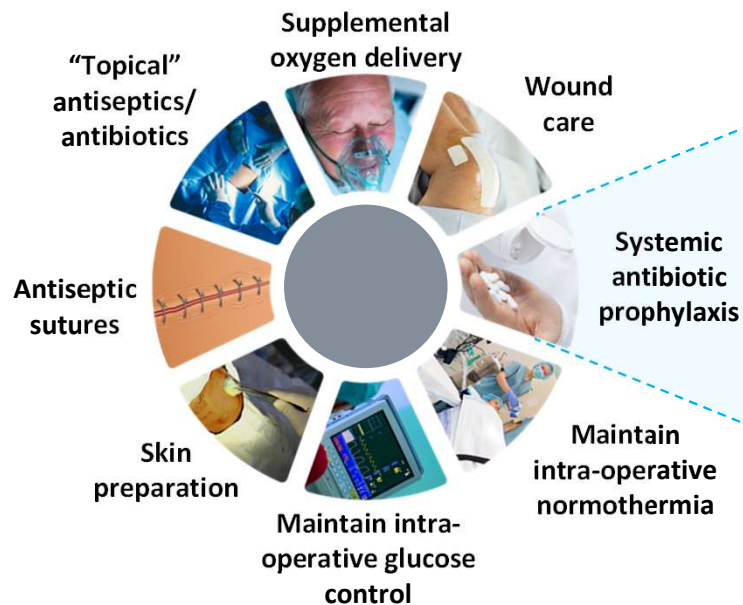


**World Health Organization**

**"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."**<sup>6</sup>

# Our Initial Focus: Enhancing Post-Operative SSI Prevention

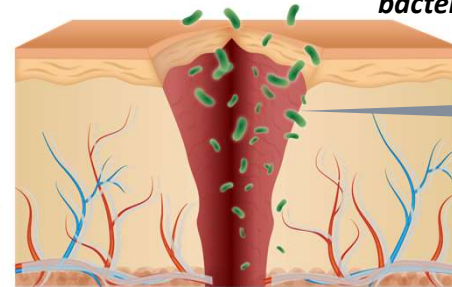
## The Current Paradigm



## Systemic Antibiotics Are Not Enough

- Systemic antibiotic prophylaxis (IV, Oral)  $\frac{1}{2}$  - 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<sup>1,2\*</sup>

*In SSIs, the surgical incision becomes contaminated by bacteria*



Our solution:  
Direct local  
antibiotic  
administration at  
the site

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

## Selected Key Players

**Medtronic**  
TYRX Absorbable  
Antibacterial Envelope

**Johnson & Johnson**  
ETHICON

**Smith+Nephew**  
PICO® 7

**3M**  
Acelity  
prevena

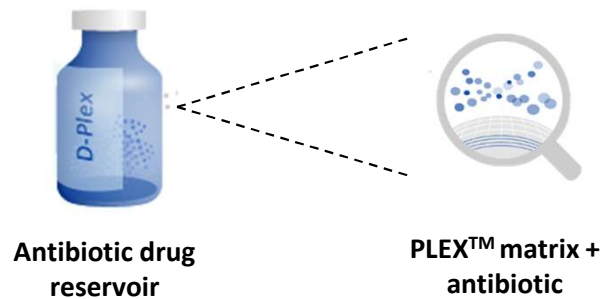
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Source: American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. Ban et al. J Am Coll Surg Vol. 224, No. 1, January 2017; New WHO recommendations on intraoperative and postoperative measures for 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-PLEX<sub>100</sub> 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-PLEX<sub>100</sub> paste in an open-heart surgery*

## D-PLEX<sub>100</sub>: locally-administered doxycycline

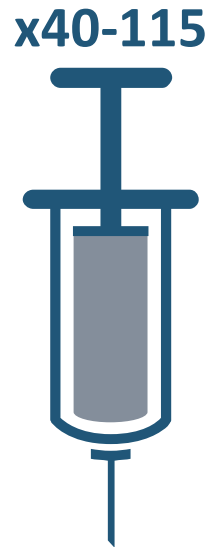
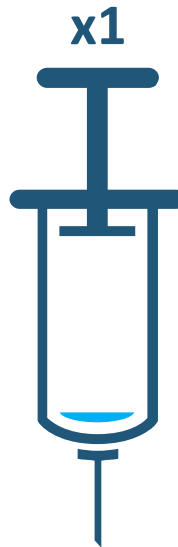
- Administered **directly in the surgical site**
- Local constant, effective concentration of antibiotic over **prolonged duration** (4 weeks)
- **Simple administration** that requires no additional training

## A Small Single Dose of D-PLEX<sub>100</sub> is Sufficient for High Local Concentrations for Several Weeks

**POLY**PID

Local delivery  
of doxycycline

55-164 mg



Systemic formulation  
of doxycycline

60 pills = 6,000 mg



D-PLEX<sub>100</sub> 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

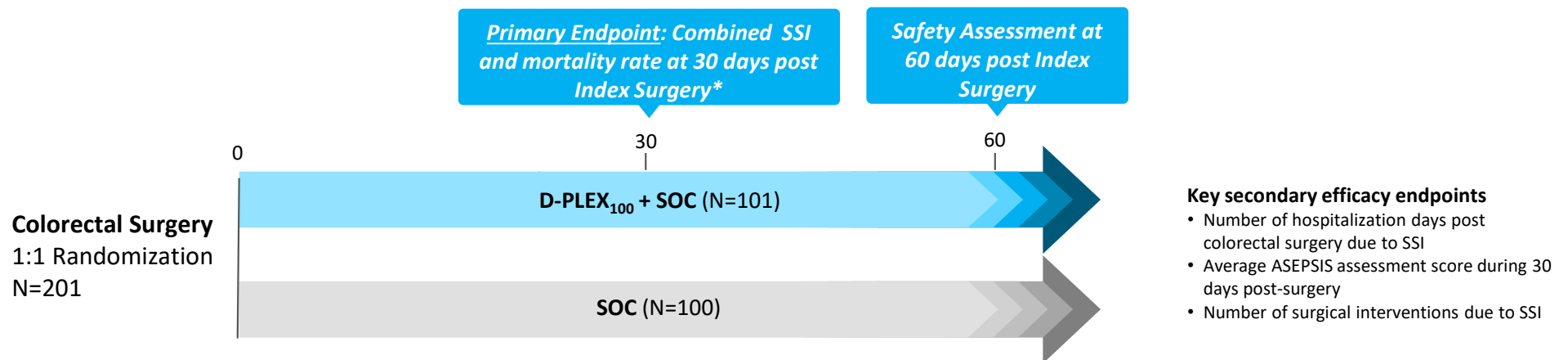
**POLY**PID

## Phase 2: D-PLEX<sub>100</sub> for the Prevention of Post Abdominal Surgery (Soft Tissue) SSIs



### Assess efficacy and safety of D-PLEX<sub>100</sub> for prevention of deep and incisional SSI after elective abdominal colon surgery

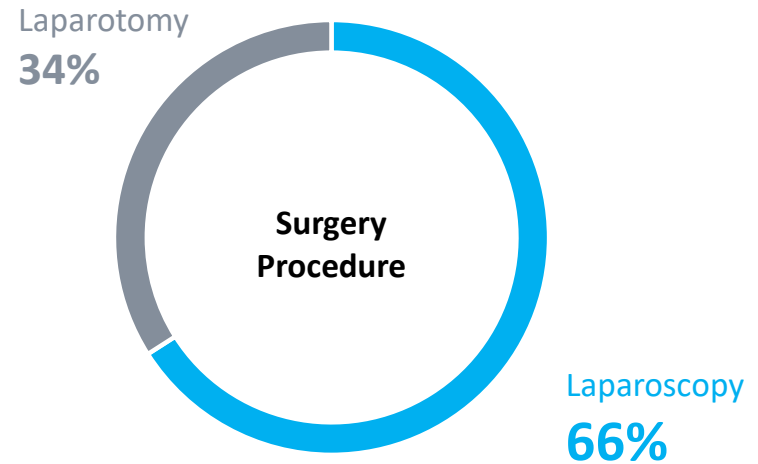
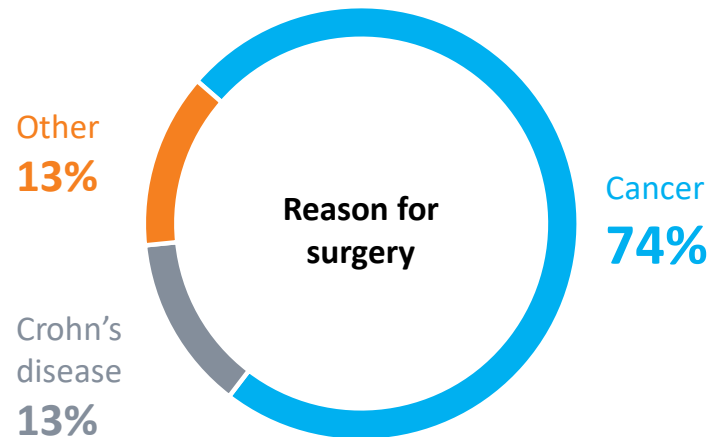
(prospective, multicenter, randomized, controlled, two arm study)





## Demographics and Baseline Data Summary Statistics

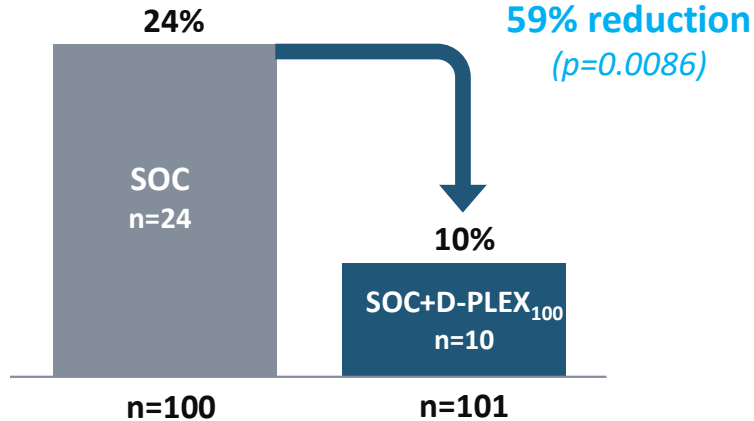
Baseline demographic (Age, BMI etc) and surgical characteristics were balanced between the two treatment groups



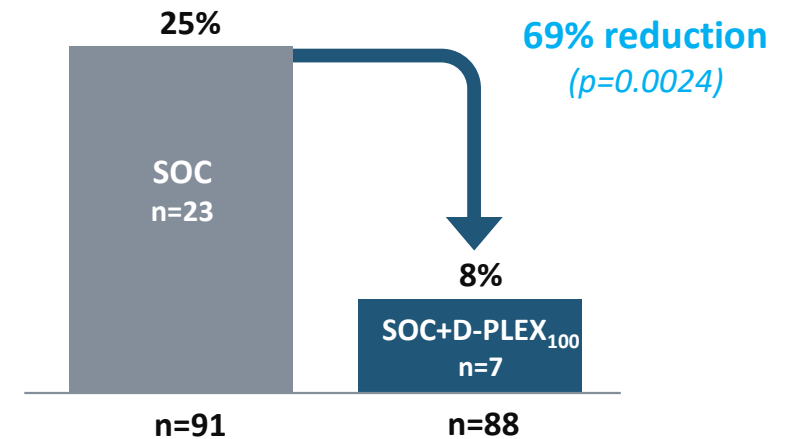


## Positive Phase 2 Results in Abdominal Surgery

### Primary Endpoint\* ITT Analysis



### Primary Endpoint - Per Protocol Analysis

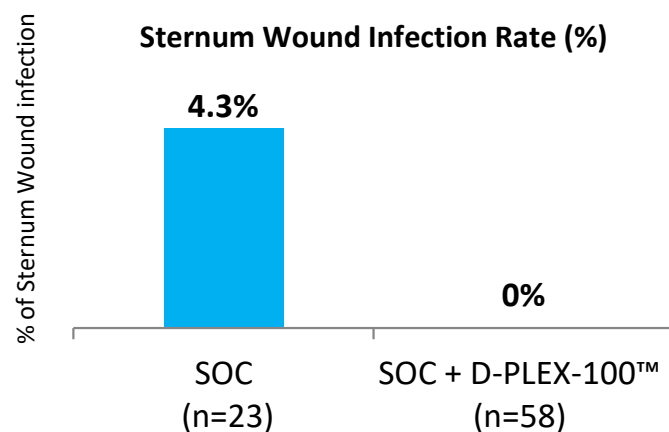


- 5 deaths observed in the SoC treatment arm, as compared to zero observed in the D-PLEX<sub>100</sub>+SOC treatment arm within the first 60 days post-surgery ( $p=0.0290$ )
- Generally well tolerated, with no confirmed drug-related SAEs and no increase in wound healing impairment at the incision site as compared to control

# D-PLEX in Sternal / Bone Surgeries



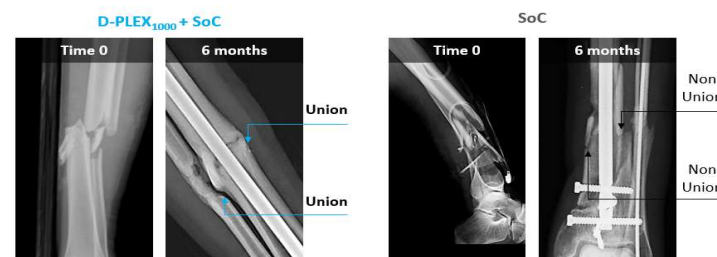
## D-PLEX<sub>100</sub>: P1b / 2 Open Heart Surgery Results<sup>1</sup>



**No Sternal Wound Infection in 58 Treated patients**  
 (Based on recent literature, we would have expected ~3-5 patients with SWIs in the D-PLEX<sub>100</sub> treatment group and 1-2 patients in the SoC control group)<sup>6-10</sup>

## D-PLEX<sub>1000</sub>: Open-Tibia Fractures<sup>11</sup>

	D-PLEX <sub>1000</sub> + SoC	SoC
Deep bone infections <sup>2</sup> / non-union <sup>3</sup> 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%<sup>4-5</sup>**

No treatment related SAEs



<sup>1</sup> Modified ITT results, based on 3 months follow-up Clinical Study Report; <sup>2</sup> One event; <sup>3</sup> Two events where another surgery and implantation of bone graft was needed; <sup>4</sup> 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; <sup>5</sup> Poletti FL et al. Current Concepts and Principles in Open Tibial Fractures - Part II Management and Controversies. 2017. <sup>6</sup> 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 <sup>7</sup> Direct sternal administration of Vancomycin and Gentamicin during closure prevents wound infection. Andreas M. et al. Interactive CardioVascular and Thoracic Surgery (2017) 1–5 <sup>8</sup> 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. <sup>9</sup> Based on 3 months follow-up interim report. <sup>10</sup> Surgical Site Infections Volume-Outcome Relationship and Year-to-Year Stability of Performance Rankings. Calderwood MS. et al. Med Care 2017;55: 79–85; <sup>11</sup> 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 DPLEX<sub>100</sub> 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-PLEX<sub>100</sub> 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 <sup>1</sup>*

# Key CMS Programs are Strong Drivers for D-PLEX<sub>100</sub>

## 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 Roll<sup>1</sup>*



Hospital	HAC penalty <sup>2</sup>	Readmission penalty <sup>2</sup>
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 Program<sup>3</sup>*

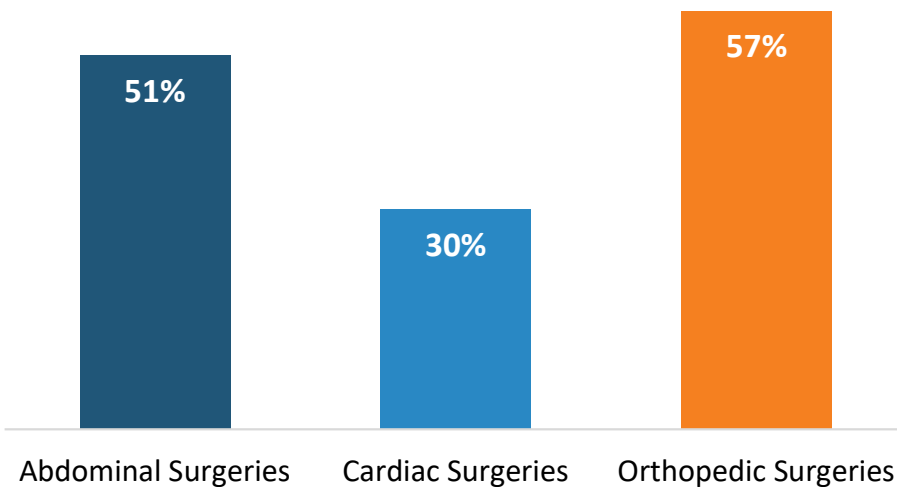
## Surgeons and non-surgeons anticipate high adoption rate of D-PLEX<sub>100</sub>

### Anticipated Use of D-Plex<sub>100</sub> By Surgery and Respondent Type

#### Surgeons

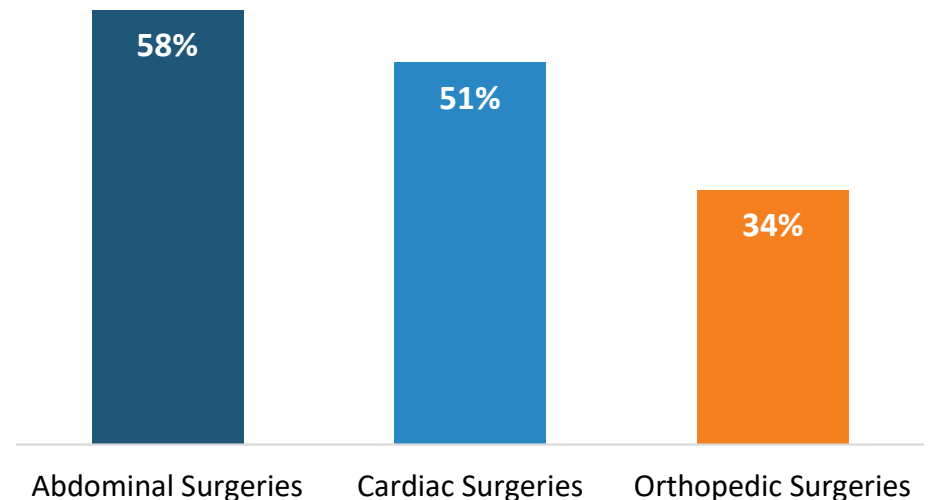
Abdominal n=17; Cardiac n=10; Orthopedic n=10

% of All Surgical Cases



#### Non-Surgeons

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



## Feedback from the market research study

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*"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