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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

96 issued patents⁽¹⁾

employees⁽²⁾

US: Summit, NJ



HQS Y Global: Petach Tikva, Israel

POLYPI

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: No Burst > Constant & linear release	D-PLEX, Sterile powder for Each vial contains 54.6 mgl (corresponds to 63.1 mg Do Storage: Refrigerate 2°C to Trial Reference Code: PILO
✓	Dosing: Varies by incision size. 1 vial >10cm, 10cm < 2vials > 20cm, 3 vials >20cm	~	Effective release rate: To overcome resistant bacteria & biofilm	Box Number: QC3566 Trial Site: N/A Investigator Name: N/A Trial subject Number: N/A



Pipeline Summary



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



¹ In December 2019, we initiated a potentially pivotal Phase 3 clinical trial of D-PLEX₁₀₀ for the prevention of sternal SSIs after cardiac surgery and, subject to feedback from the FDA, we plan to continue development of D-PLEX₁₀₀ for the prevention of SSIs in patients undergoing abdominal surgery. We intend to pursue a broad label for D-PLEX₁₀₀ for the prevention of SSIs, the scope of which will depend on the clinical data generated from our potentially pivotal Phase 3 clinical trials and discussions with the FDA and the EMA.

6

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



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."



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

\$11k-26k

Cost of treatment per infection directly attributable to SSIs



2-11x

S10bn

US

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

EU

Estimated SSI-related incremental

annual hospital costs in the US and EU^{4, 5}

~€11bn







"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



¹ Deverickl 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 SIs become evident only after a patient has been discharged.³ Financial Impact of Surgical Site Infections on Hospitals. John Shepard and al. JAMA Surg. 2013;148(10):009:2141. https://dow.co.acetideents.com/www.2018/2/6/16/16/80406/hin.schwarevealch.ins.urgene-complications.⁴Surgical Site Infection. Surgical Site Infection and Hospitals Infection. Surgical Site Infection and Hospitals Infection. Surgical Site Infection and Hospitals. John Shepard and al. JAMA Surg. 2013;148(10):092:914. https://dow.co.acetideents.com/www.2018/2/6/16/16/80406/hin.schwarevealch.ins.urgene-complications.⁴Surgical Site Infection. Surgical Site Infection. Surgical



Our Initial Focus: Enhancing Post-Operative SSI Prevention



Systemic Antibiotics Are Not Enough

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





Our solution: <u>Direct local</u> <u>antibiotic</u> <u>administration</u> at the site

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 durina closure prevents wound infection. Andreas M. et al. Interactive Cardio/asculor and Thoracic Surgery (2017) 1–5.

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

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



Antibiotic drug reservoir





Example of surgeon spreading the D-PLEX₁₀₀ paste in an openheart 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



Source: BCC research report

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



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



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)



Key secondary efficacy endpoints

- Number of hospitalization days post colorectal surgery due to SSI
- Average ASEPSIS assessment score during 30 days post-surgery
- Number of surgical interventions
 due to SSI



sSI include Superficial and Deep SSIs ; Combined primary endpoint as confirmed by a Blinded and independent adjudication committee.

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





- 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

PEP is the Combined SSI and mortality rate which is measured by the number and proportion of subjects with either an SSI event (as determined by the abdominal surgery) or mortality or any reason within 30 days

rrent standard of care for preventing SSIs involves the implementation of a range of treatment and prevention measures before, during and after surgery, including prophylactic antibiotic administration, antiseptic measures and wound care.

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 TT 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 Debridment of Open Tibial Fractures: A Systematic Review and Meta-Analysis of Infection and Nonunian Rates. 2016; ⁵ Poletti FL et al. Current Concepts and Principles in Open Tibial Tractures: Part II Management and Controversies. 2017. ⁶ Adding vancomycin to perioparitive prophylaxis decreases deep stemal wound infections in high-risk cardiac surgery patients. Reneike S. et al. European Journal of Cardio-Thoracic Surgery (2017) 1–7² Direct sternal administration of Vancomycin and Reinopean Journal of Cardio-Thoracic Surgery (2017) Horizon Competent and Thoracic Surgery (2017) 1–5³ 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) 1–6³. 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







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



- 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 1,2



based on Current Clinical Development program and regulatory strategy ; ² Mainly major Open-surgeries (except for Colorectal Surgeries).

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)

BEST HOSPITAL

USNew

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 ³
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 Program⁴



Source: 1) Preeminent Hospitals Penalized Over Rates Of Patients' Injuries, Kaiser Health News, <u>https://tinyurl.com/y5863xtl</u> 2)The advisory Board, <u>www.advisory.com/daily-briefing/2020/02/03/hac-penalizes</u> 3) <u>https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program 4</u>) https://www.beckershospitalreview.com/finance/cms-penalizes-2-583-hospitals-for-highreadmissions-5-things-to-know.html

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 nearterm value creation



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

