PolyPid Announces Publication in International Journal of Surgery Highlighting Results of Phase 3 SHIELD I Trial of D-PLEX in Prevention of Surgical Site Infections in Abdominal Colorectal Surgery

SHIELD I Study is One of the Largest Phase 3 Trials in the Prevention of SSIs in Colorectal Resection Conducted in Over a Decade

Pre-Specified and Post-Hoc Analyses Suggested that D-PLEX$_{100}$ May Benefit Patients with Increased SSI Risk, Including Those with Lengthy Incisions

SHIELD II Study, the Ongoing Second Phase 3 with D-PLEX$_{100}$, Focuses on Patients with Large Surgical Incisions; Top-line Results Expected in Q1 2025

PETACH TIKVA, Israel, Oct. 21, 2024 — PolyPid Ltd. (Nasdaq: PYPD) ("PolyPid" or the "Company"), a late-stage biopharma company aiming to improve surgical outcomes, today announced a publication in the *International Journal of Surgery* (*IJS*) titled, "*Effect of Local Prolonged-Release Incisional Doxycycline on Surgical Site Infection Prophylaxis in Abdominal Colorectal Surgery: The SHIELD I Randomized Clinical Trial*." The article highlights the full dataset from the first Phase 3 study (NCT04233424) of D-PLEX$_{100}$, from which top-line results were announced in September 2022.

"The overall infection rate in SHIELD I was significantly impacted by the COVID-19-related safety restrictions introduced in the surgical setting during the pandemic," said Prof. Oded Zmora, Professor of Surgery at the Shamir Medical Center in Tel Aviv Israel, and President of the European Society of Coloproctology. "Given this unexpected change in baseline infection rate, the SHIELD I primary outcome became extraordinarily difficult to meet. For this reason, while the SHIELD I study did not achieve its primary endpoint, both pre-specified and post-hoc analyses suggested that D-PLEX$_{100}$ may benefit patients at increased risk of surgical site infections (SSIs), including those with lengthy incisions. While SHIELD II is ongoing, the clinical data generated by D-PLEX$_{100}$ to date suggest it may be a promising future adjunctive component of surgical care bundles."

A virtual KOL event hosted by the Company in June 2024, highlighted that procedural and patient-related risk factors, such as smoking, alcohol abuse, type 2 diabetes and a high BMI, are known to have a significant negative impact on the risk of developing an SSI, and this increase in risk is compounded when patients have multiple risk factors. During the presentation, Prof. Charles E. Edmiston, Emeritus Professor of Surgery, Division of Vascular Surgery, Medical College of Wisconsin, also confirmed that the long-term cost of SSIs to commercial payers is substantial and concluded there remains a significant unmet need for additional measures that prevent the development of SSIs.

“We are thrilled to have the SHIELD I study results published in the highly regarded *International Journal of Surgery*, ranked second out of 212 titles in the Surgery category by impact factor[1]. Importantly, in the post-COVID-19 setting, we are seeing infection rates normalize to levels on par with those prior to the pandemic. We expect the SHIELD II infection rate to be more in line with the pre-pandemic rate and remain encouraged by the data generated in the SHIELD I pre-specified subgroup analysis that evaluated the primary endpoint in patients with incision lengths over 20 cm, which showed a 54% reduction in SSI rates between the D-PLEX$_{100}$ treatment arm and the control arm,” said Dikla Czaczkes Akselbrad, PolyPid’s Chief Executive Officer. “Earlier this month, we enrolled the last patient required to conduct the planned SHIELD II unblinded interim analysis, which is anticipated to occur later this quarter and will be followed by the availability of top-line results, expected in the first quarter of 2025.”

Phase 3 SHIELD I Trial Results

The *IJS* article presents results of the Phase 3 SHIELD I trial **(S**urgical site **H**ospital acquired **I**nfection pr**E**vention with **L**ocal **D**-PLEX), a prospective, multinational, randomized, double blind Phase 3 trial designed to assess the efficacy and safety of D-PLEX$_{100}$ administered concomitantly with standard of care (SoC), which included prophylactic systemic antibiotics, compared to a SoC alone arm, in prevention of post-abdominal surgery incisional infection. The primary endpoint of the trial was the combination of incisional SSIs, incisional reinterventions due to suspected SSI or to poor wound healing including wound dehiscence, as determined by a blinded and independent adjudication committee, and mortality for any reason within 30 days post-surgery. The trial enrolled 977 patients, with 488 in the D-PLEX$_{100}$ arm and 489 in the SoC arm, from more than 60 centers in the United States, Europe and Israel.

- A total of 104 patients experienced a primary outcome event: 45/485 (9.3%) in D-PLEX$_{100}$ versus 59/489 (12.1%) in SoC. The clinically meaningful 23% event reduction in the D-PLEX$_{100}$ treatment arm was not statistically significant (p=0.1520).
- In the greater than 20 cm incision length pre-specified subgroup, a statistically significant 54% reduction in primary outcome events was observed in D-PLEX$_{100}$ (8%, 17/212) compared with SoC (17.5%, 37/211, p=0.0032).
- Analysis of the key secondary efficacy outcome, incisional SSI, also indicated a 54.6% reduction in the greater than 20 cm incision subgroup (4.4% in D-PLEX$_{100}$ vs. 9.7% in SoC, p= 0.0410).
- Exploratory analysis of the additional secondary efficacy outcomes indicated marked differences in favor of D-PLEX$_{100}$ vs. SoC in the greater than 20 cm incision length subgroup. Notably, the need for any surgical reintervention decreased by 54.6% in the D-PLEX$_{100}$ treatment arm compared to the SOC arm (4.4% vs. 9.7%, p= 0.0333).
- There were no safety concerns raised by the independent Data Safety Monitoring Board

in SHIELD I. The overall incidence of treatment emergent adverse events (TEAEs) was similar between the study arms, with numerically lower incidences of severe and serious TEAEs, and any TEAEs requiring surgical reinterventions in the D-PLEX$_{100}$ arm compared to the SoC arm.

About SHIELD II

SHIELD II is a prospective, multinational, randomized, double blind Phase 3 trial designed to assess the efficacy and safety of D-PLEX$_{100}$ administered concomitantly with SoC, which includes prophylactic systemic antibiotics, compared to SoC alone arm, in the prevention of post abdominal-surgery incisional infection in patients undergoing surgeries with incisions greater than 20 cm. The primary endpoint of the trial is measured by the proportion of subjects with either an SSI event as determined by a blinded and independent adjudication committee, reintervention, or mortality for any reason within 30 days post-surgery. Patient safety will be monitored for an additional 30 days. The trial will enroll patients in centers in the United States, Europe and Israel.

About D-PLEX$_{100}$

D-PLEX$_{100,}$ PolyPid's lead product candidate, is designed to provide local prolonged and controlled anti-bacterial activity directly at the surgical site to prevent SSIs. Following the administration of D-PLEX$_{100}$ into the surgical site, the PLEX (Polymer-Lipid Encapsulation matriX) technology pairs with Active Pharmaceutical Ingredients, enabling a prolonged and continuous release of the broad-spectrum antibiotic doxycycline, resulting in a high local concentration of the drug for a period of 30 days for the prevention of SSIs, with additional potential to prevent SSIs caused by antibiotic-resistant bacteria at the surgical site. D-PLEX$_{100}$ received Breakthrough Therapy Designation from the U.S. Food and Drug Administration for the prevention of SSIs in patients undergoing elective colorectal surgery. D-PLEX$_{100}$ is currently in Phase 3 SHIELD II trial for the prevention of surgical site infections in patients undergoing abdominal colorectal surgery with large incisions.

About PolyPid

PolyPid Ltd. (Nasdaq: PYPD) is a late-stage biopharma company aiming to improve surgical outcomes. Through locally administered, controlled, prolonged-release therapeutics, PolyPid's proprietary PLEX (Polymer-Lipid Encapsulation matriX) technology pairs with Active Pharmaceutical Ingredients (APIs), enabling precise delivery of drugs at optimal release rates over durations ranging from several days to months. PolyPid's lead product candidate D-PLEX$_{100}$ is in Phase 3 clinical trial for the prevention of abdominal colorectal surgical site infections. In addition, the Company is currently in preclinical stages to test the efficacy of OncoPLEX for the treatment of solid tumors, beginning with glioblastoma.

For additional Company information, please visit http://www.polypid.com and follow us on Twitter and LinkedIn.

Forward-looking Statements

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act and other securities laws. Words such as “expects,” “anticipates,” “intends,” “plans,” “believes,” “seeks,” “estimates” and similar expressions or variations of such words are intended to identify forward-looking statements. For example, the Company is using forward-looking statements when it discusses potential benefits and advantages of D-PLEX$_{100}$, that D-PLEX$_{100}$ may be a promising future adjunctive component of surgical care bundles, the Company’s expectation that the SHIELD II infection rate will be more in line with the pre-pandemic rates, total recruitment time into the SHIELD II study and the timing of the top-line results and an unblinded interim analysis. Forward-looking statements are not historical facts, and are based upon management’s current expectations, beliefs and projections, many of which, by their nature, are inherently uncertain. Such expectations, beliefs and projections are expressed in good faith. However, there can be no assurance that management’s expectations, beliefs and projections will be achieved, and actual results may differ materially from what is expressed in or indicated by the forward-looking statements. Forward-looking statements are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in the forward-looking statements. For a more detailed description of the risks and uncertainties affecting the Company, reference is made to the Company’s reports filed from time to time with the Securities and Exchange Commission (“SEC”), including, but not limited to, the risks detailed in the Company’s Annual Report on Form 20-F filed on March 6, 2024. Forward-looking statements speak only as of the date the statements are made. The Company assumes no obligation to update forward-looking statements to reflect actual results, subsequent events or circumstances, changes in assumptions or changes in other factors affecting forward-looking information except to the extent required by applicable securities laws. If the Company does update one or more forward-looking statements, no inference should be drawn that the Company will make additional updates with respect thereto or with respect to other forward-looking statements.

References and links to websites have been provided as a convenience, and the information contained on such websites is not incorporated by reference into this press release. PolyPid is not responsible for the contents of third-party websites.

Contacts:

PolyPid Ltd.
Ori Warshavsky
COO – US
908-858-5995
IR@Polypid.com

Investors:

Brian Ritchie

LifeSci Advisors
212-915-2578
BRitchie@lifesciadvisors.com

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[1] Based on OOIR.org https://ooir.org/journals.php?field=Clinical+Medicine&category=Surgery&metric=jif