PolyPid Announces Top-line Results of Phase 3 SHIELD I Trial of D-PLEX for the Prevention of Surgical Site Infections in Abdominal Surgery

SHIELD I Study did not Achieve its Primary Endpoint of Reduction in Surgical Site Infections and Mortality

In an FDA Requested Pre-specified Subgroup Analysis in Subjects with Incision Lengths over 20 centimeters (n=423), D-PLEX$_{100}$ + SoC Achieved a Statistically Significant Reduction of 54 percent on the Primary Endpoint versus SoC alone (p<0.0032)

PETACH TIKVA, Israel, Sept. 02, 2022 — PolyPid Ltd. (Nasdaq: PYPD) ("PolyPid" or the "Company"), a late-stage biopharma company aiming to improve surgical outcomes, today announced top-line results from the SHIELD I Phase 3 study of D-PLEX$_{100}$ for the prevention of surgical site infections (SSIs) in abdominal surgery.

SHIELD I (Surgical site Hospital acquired Infection prEvention with Local D-PLEX$_{100}$) is 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) compared to a SoC alone arm, in the prevention of post-abdominal surgery incisional infection. The primary endpoint of the trial is the combination of incisional SSIs and mortality as measured by the proportion of subjects with either an SSI event, as determined by a blinded and independent adjudication committee, or mortality for any reason within 30 days post-surgery. The SHIELD I study is designed to demonstrate at least a 50 percent reduction in incisional SSIs in the D-PLEX$_{100}$ treatment arm compared to the control arm, with 90 percent power and a maximum alpha level of 0.0487. A total of 977 patients were randomized into the study, consisting of 488 subjects in the D-PLEX$_{100}$ treatment arm and 489 patients in the control arm.

In the Intent to Treat (ITT) population, the local administration of D-PLEX$_{100}$ and SoC (n=485) resulted in a decrease in SSIs and mortality of 23 percent compared to SoC alone (n=489) (p=0.1520). Within the first 30 days post-surgery, there were 15 deaths in the SoC treatment arm, as compared to 11 in the D-PLEX$_{100}$ treatment arm. The local administration of D-PLEX$_{100}$ as compared to SoC alone also did not achieve statistical significance on the key secondary endpoint evaluating SSI events within 30 days post-abdominal index surgery.

In a pre-specified subgroup ITT analysis requested by the U.S. Food and Drug Administration (FDA) of a total of 423 subjects with incision lengths >20 centimeters, the local administration of D-PLEX$_{100}$ resulted in a statistically significant reduction of 54 percent on the primary endpoint, compared to SoC alone (p<0.0032). Within the first 30 days post-surgery, SSIs decreased from 8.5% in the SoC treatment arm (n=211), as compared to 4.2% in the D-PLEX$_{100}$ treatment arm (n=212).

“While these top-line results did not meet our expectations following the highly compelling positive data generated in our Phase 2 study, we remain confident in the future potential of D-PLEX$_{100}$,” said Dikla Czaczkes Akselbrad, PolyPid’s Chief Executive Officer. “The SHIELD I study, while well-executed and balanced, had a significantly lower SSI rate in the SoC treatment arm of 6.3% percent, as compared to mid-teens percentage infection rate for colorectal surgeries according to published literature at the time of the study design. The overall infection rate in SHIELD I was meaningfully impacted by the COVID-19-related safety restrictions introduced in the surgical setting during that time, a factor that decreased the infection rate in surgical procedures during the COVID-19 pandemic. The low infection rate in the SoC treatment arm of the trial, significantly below historical infection rates consistent with colorectal cancer procedures, established a low baseline from which it was highly challenging to show a significant effect on SSIs. Looking ahead, we are encouraged by the data generated in the pre-specified subgroup analysis that evaluated the primary endpoint in subjects with incision lengths over 20 centimeters, which demonstrated a 54 percent reduction in SSI rates between the D-PLEX$_{100}$ treatment arm and the control arm. We intend to further assess the collective results of SHIELD I and discuss the COVID-19 driven lower than anticipated overall infection rate in the study with the FDA, as we determine the appropriate next steps for D-PLEX$_{100}$ for the prevention of SSIs in abdominal surgery. On behalf of the PolyPid team, I would like to thank the patients and physicians who participated in SHIELD I.”

There were no safety concerns raised by the independent Data Safety Monitoring Board in SHIELD I. PolyPid intends to present the full top-line results from SHIELD I at a future medical meeting.

The Company’s second Phase 3 trial of D-PLEX$_{100}$ for the prevention of SSIs in abdominal surgery, SHIELD II, which incorporates broader eligibility criteria, is ongoing and has enrolled over 200 subjects to date. Based on the overall data generated in SHIELD I, PolyPid intends to discuss the results with the FDA and evaluate the appropriate next steps for SHIELD II.

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 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. FDA for the prevention of SSIs in patients undergoing elective colorectal surgery. D-PLEX$_{100}$ also received three Qualified Infectious Disease Product (QIDP) designations, and three Fast Track designations for the

prevention of SSIs in patients undergoing elective colorectal surgery, post-abdominal surgery incisional infection and for the prevention of sternal wound infection post-cardiac surgery.

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 trials for the prevention of soft tissue abdominal and sternal surgical site infections. In addition, the Company is currently in preclinical stages to test the efficacy of OncoPLEX for 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 its ongoing clinical trials, its intention to further assess the collective results of SHIELD I and discuss the COVID-19 driven lower than anticipated overall infection rate in the study with the FDA, as it determines the appropriate next steps for D-PLEX$_{100}$ for the prevention of SSIs in abdominal surgery, its intention to present the full top-line results from SHIELD I at a future medical meeting and its intention to discuss the results with the FDA and evaluate the appropriate next steps for SHIELD II. 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 February 28, 2022. 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.

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