PolyPid Announces Recruitment of First Patient in Revised SHIELD II Phase 3 Trial Evaluating D-PLEX for Prevention of Abdominal Colorectal Surgical Site Infections

Company Recently Reached Agreement with FDA on Design of Trial

Top-line Results Expected in Mid-2024

PETACH TIKVA, Israel, June 22, 2023 — PolyPid Ltd. (Nasdaq: PYPD) ("PolyPid" or the "Company"), a late-stage biopharma company aiming to improve surgical outcomes, today announced that the first patient has been recruited and is scheduled for surgery in its revised SHIELD II Phase 3 trial evaluating D-PLEX$_{100}$ for the prevention of abdominal colorectal surgical site infections (SSIs). The U.S. Food and Drug Administration (FDA) recently accepted the Company's revised protocol for SHIELD II, which is recruiting patients undergoing colorectal resection surgery with large incisions (> 20 cm).

SHIELD II will enroll an estimated 550 additional patients beyond the 40 patients already recruited into the trial. Total recruitment time into the trial is anticipated to be approximately 12 months and top-line results are expected in mid-2024. PolyPid also intends to conduct an unblinded interim analysis once a total of approximately 400 patients complete their 30-day follow-up.

"The recruitment of the first patient in the revised SHIELD II trial represents a significant milestone for our promising late-stage D-PLEX$_{100}$ development program and our company," stated Dikla Czaczkes Akselbrad, PolyPid's Chief Executive Officer. "The revised SHIELD II protocol is focused on the population of patients undergoing surgeries with large incisions, which showed a highly statistically significant reduction of 54% in SSIs in SHIELD I. To further de-risk the trial, SHIELD II will primarily be conducted in the best performing sites from SHIELD I as it relates to recruitment, patient monitoring and good clinical practice, and we have enhanced our internal clinical operations capabilities. We are excited to resume the SHIELD II trial and look forward to providing updates on its progress in the coming months."

About SHIELD II

SHIELD II (Surgical site Hospital acquired Infection prEvention with Local D-PLEX) 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), 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 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 a 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 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 the ability of D-PLEX$_{100}$ to prevent SSIs, the expected total recruitment and timing of recruitment for the SHIELD II Phase 3 trial, the effectiveness of measures to de-risk the trial and the timing of top-line results therefrom and potential 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 31, 2023. 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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