

PolyPid Announces Successful Completion of Enrollment in Phase 3 SHIELD II Trial of D-PLEX for the Prevention of Abdominal Colorectal Surgical Site Infections

Last Patient Enrolled Following Positive Recommendation by DSMB to Conclude Enrollment of Phase 3 Trial at 800 Patients; Top-line Results Expected by End of Q2 2025 and, if Positive, Expected to be Followed by Submission of an NDA to the FDA Leveraging the Company's Fast-Track and Breakthrough Therapy Designations

PETACH TIKVA, Israel, March 11, 2025 — PolyPid Ltd. (Nasdaq: PYPD) ("PolyPid" or the "Company"), a late-stage biopharma company aiming to improve surgical outcomes, today announced the successful completion of enrollment in the SHIELD II Phase 3 trial for D-PLEX₁₀₀ for the prevention of surgical site infections in patients undergoing abdominal colorectal surgery. This milestone follows recommendation by the independent Data Safety Monitoring Board ("DSMB"), which, after analyzing unblinded efficacy data from the first 430 enrolled patients in the trial, recommended concluding the study upon enrollment of 800 patients, the lowest sample size reassessment stop after the minimum planned number of patients.

The Company anticipates reporting top-line results by the end of the second quarter of 2025. If the Phase 3 data are positive, PolyPid expects to submit a New Drug Application ("NDA") to the U.S. Food and Drug Administration ("FDA"), leveraging the FDA's Fast Track and Breakthrough Therapy designations.

"We are excited to reach another critical milestone in our ongoing SHIELD II Phase 3 trial, reinforcing the positive trajectory of D-PLEX₁₀₀'s development," said Dikla Czaczkes Akselbrad, PolyPid's Chief Executive Officer. "With top-line data expected by the end of the second quarter of 2025, we are preparing to engage with the FDA for a pre-NDA meeting to discuss a rolling NDA submission under the Breakthrough Therapy designation. Importantly, we remain in active discussions with multiple potential partners for the commercialization of D-PLEX₁₀₀ in various regions, starting with the U.S."

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-PLEX₁₀₀ 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 abdominal colorectal surgeries with large incisions. The primary endpoint of the trial is measured by the proportion of subjects with either a surgical site infection ("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-PLEX₁₀₀

D-PLEX₁₀₀, 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-PLEX₁₀₀ 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-PLEX₁₀₀ received Breakthrough Therapy, Fast Track and Qualified Infectious Disease Product (QIDP) designations from the FDA for the prevention of SSIs in patients undergoing abdominal colorectal surgery. D-PLEX₁₀₀ 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-PLEX₁₀₀ 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 the timing of anticipated reporting of top-line results, that upon potential positive Phase 3 data, the Company anticipates submission of an NDA leveraging the advantages of Fast Track and Breakthrough Therapy designations, the intention to pursue a pre-NDA meeting with the FDA to discuss a rolling NDA submission, and discussions with multiple potential partners for the commercialization of D-PLEX₁₀₀ in various regions, starting with the U.S. 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, including, but not limited to, the risks detailed in the Company's Annual Report on Form 20-F filed on February 26, 2025. 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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