PolyPid Initiates SHIELD II: Second Phase 3 Clinical Trial of D-PLEX for the Prevention of Post-Abdominal Surgery Incisional Infections

Enrollment in SHIELD I, the First Phase 3 Clinical Trial Continues to Progress, with Top-line Data Anticipated in Second Half of 2021

PETAH TIKVA, Israel, Dec. 16, 2020 — PolyPid Ltd. (Nasdaq: PYPD), a Phase 3 clinical-stage biopharmaceutical company focused on developing targeted, locally administered and prolonged-release therapeutics using its proprietary PLEX technology, today announced that the first patient has been enrolled and randomized in the SHIELD II (**S**urgical site **H**ospital acquired **I**nfection pr**E**vention with **L**ocal **D**-plex) trial, the Company's second of two Phase 3 clinical trials for its lead product candidate, D-PLEX$_{100}$, for the prevention of post-abdominal surgery incisional infection (soft tissue).

"Three weeks after D-PLEX100 received Breakthrough Therapy Designation from the FDA, the enrollment of the first patient in our second Phase 3 trial is a significant achievement for our D-PLEX$_{100}$ clinical development program. Importantly, SHIELD II will have broader eligibility criteria than SHIELD I, with the inclusion of minimally invasive surgical procedures, providing additional clinical evaluation of the potential of D-PLEX$_{100}$ to prevent surgical site infections (SSIs) in broader target populations," said Amir Weisberg, PolyPid's CEO. "Enrollment in our first Phase 3 clinical trial, SHIELD I, continues to progress as expected and we anticipate the availability of top-line results from this study in the second half of next year. SHIELD I and SHIELD II will serve as the basis for our first New Drug Application submission."

"Based on the compelling data generated to date, D-PLEX$_{100}$, if approved, has the potential to be a highly effective solution in preventing SSIs, even in the most complex surgical settings such as abdominal surgery with colorectal resection," said Anthony Senagore, M.D., a leading colorectal surgeon, and a medical advisor to PolyPid. "As systemic antibiotic penetration into the surgical wound is significantly limited due to blood flow interruption, a substantial unmet need remains in preventing SSIs. I look forward to the continued clinical assessment of this promising therapeutic candidate in the SHIELD I and SHIELD II studies."

SHIELD II (NCT04411199) is a prospective, multinational, multicenter, randomized, double-blind Phase 3 trial designed to assess the efficacy and safety of D-PLEX$_{100}$ administered concomitantly with the Standard of Care (SoC), compared to a SoC-treated control arm, for the prevention of post-abdominal surgery incisional infection. The primary endpoint of the trial is the infection rate, as measured by the proportion of subjects with at least one abdominal target incisional infection event within 30 days post-abdominal surgery, determined by a blinded independent adjudication committee. The trial will enroll a minimum of 900 patients, with a maximum of approximately 1,400 subjects, as defined by the adaptive study design, in approximately 60 centers in the United States, Europe and Israel.

About D-PLEX$_{100}$

PolyPid's lead product candidate, D-PLEX$_{100}$, is a novel drug product candidate 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 technology enables a prolonged and constant release of the broad-spectrum antibiotic doxycycline, resulting in high local concentration of the drug for a period of four weeks for the prevention of SSIs, with additional potential to prevent SSIs caused by antibiotic-resistant bacteria at the surgical site. D-PLEX$_{100}$ has received Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA) for the prevention of SSIs in patients undergoing elective colorectal surgery. D-PLEX$_{100}$ has also received two Qualified Infectious Disease Product (QIDP) designations as well as two Fast Track designations for the prevention of post-abdominal surgery incisional infection and for the prevention of sternal wound infection post-cardiac surgery.

About PolyPid

PolyPid is a Phase 3 clinical-stage biopharmaceutical company focused on developing targeted, locally administered and prolonged-release therapeutics using its proprietary PLEX (Polymer-Lipid Encapsulation matriX) technology. PolyPid's product candidates are designed to address diseases with high unmet medical needs by pairing PLEX with drugs to deliver them directly to precise sites in the body at predetermined release rates and over durations ranging from several days to several months. PolyPid's lead product candidate, D-PLEX$_{100}$, is in Phase 3 clinical trials for the prevention of sternal SSIs and abdominal SSIs. PolyPid's technology and products are based on the inventions and the professional leadership of Dr. Noam Emanuel, the Founder and the Chief Scientific Officer of the company.

For additional company information, visit www.polypid.com.

Forward-looking Statements

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 and other Federal 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, PolyPid is using forward-looking statements in this press release when it discusses the potential of D-PLEX$_{100}$ to prevent SSIs, and the enrollment and timing of clinical trials. Because such statements deal with future events and are based on PolyPid's current expectations, they are subject to various risks and uncertainties. Also, while PolyPid has received Fast Track Designation for D-PLEX$_{100}$ for the prevention of SSIs, it cannot guarantee that it will be able to maintain such designation due to reasons within our outside of its control. Actual results, performance or achievements of

PolyPid could differ materially from those described in or implied by the statements in this press release. The forward-looking statements contained or implied in this press release are subject to other risks and uncertainties, including those discussed under the heading “Risk Factors” in PolyPid’s final prospectus dated June 25, 2020, filed pursuant to Rule 424(b)(4) with the Securities and Exchange Commission (SEC), and in any subsequent filings with the SEC. Except as otherwise required by law, PolyPid undertakes no obligation to publicly release any revisions to these forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. 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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