

BeyondSpring Announces \$35.4 Million Sale of a Portion of Equity Interest in SEED Therapeutics to Advance Lead Asset Plinabulin to Anti-Cancer Registrational Studies

FLORHAM PARK, N.J., Jan. 28, 2025 (GLOBE NEWSWIRE) -- **BeyondSpring Inc.** (NASDAQ: BYSI) (“BeyondSpring” or the “Company”), a global clinical-stage biopharmaceutical company developing innovative cancer therapies, today announced that it has entered into definitive agreements to sell a portion of its Series A-1 Preferred Shares of SEED Therapeutics Inc. (“SEED”), a biotechnology company focused on Targeted Protein Degradation (TPD) technology and a subsidiary of the Company, for gross proceeds of approximately \$35.4 million. Upon completion of the transactions, BeyondSpring, together with SEED Technology Limited, a majority-owned indirect subsidiary of the Company, is expected to retain approximately 14.4% of SEED’s outstanding shares.

Strategic Background and Rationale

Since 2016, BeyondSpring has been at the forefront of TPD innovation, incubating its proprietary TPD technology internally and co-founding SEED with Eli Lilly and Company in 2020. Through this pioneering sponsorship, SEED has grown into a leader in TPD, a revolutionary drug discovery approach targeting previously undruggable proteins. SEED has developed a robust pipeline of therapies in oncology and neurodegeneration, leveraging its proprietary molecular glue-based platform. Research collaborations with Eli Lilly and Company, and Eisai Co. Ltd. (“Eisai”) further validate its leadership in TPD.

The recent Series A-3 financing led by Eisai, at a pre-money valuation of \$100 million, underscores SEED’s innovation and market potential. The transactions announced today will enable BeyondSpring to unlock value while retaining a meaningful ownership stake in SEED. The \$35.4 million in proceeds will advance BeyondSpring’s late-stage clinical trials of its lead asset, Plinabulin, ensuring critical resources without diluting shareholder equity.

Plinabulin: A First-in-Class Agent with Broad Potential

Plinabulin is a first-in-class anti-cancer agent which has been used in over 700 cancer patients with good tolerability. It is a differentiated tubulin binder, which releases immune defense protein GEF-H1, leading to dendritic cell maturation that drives both direct anti-cancer activity and immune system activation^{1,2}. It has demonstrated durable anti-cancer benefits across multiple clinical studies and addresses significant unmet medical needs in oncology:

- **DUBLIN-3 (103) Study** (Sept. 2024): In a global phase 3 study (n=549)³, Plinabulin combined with docetaxel achieved significant overall survival benefit, and doubling 2-year and 3-year survival rate in second- and third-line non-small-cell lung cancer (NSCLC) with EGFR wild type, compared to docetaxel alone (Press Release Link).
- **303 Study** (Nov. 2024): Plinabulin combined with pembrolizumab and docetaxel achieved an 89.3% disease control rate and a median progression-free survival (PFS) of 8.6 months in 30 NSCLC patients who progressed on immune checkpoint inhibitors (Press Release Link).
- **302 Study** (Mar. 2024): Enrollment began for first-line extended-stage small cell lung cancer (ES-SCLC) patients treated with Plinabulin, etoposide, platinum therapy, and pembrolizumab (Press Release Link).

Dr. Trevor Feinstein, MD, a lead principal investigator of the DUBLIN-3 Study at Piedmont Cancer Center, Atlanta, highlighted the critical need addressed by Plinabulin:

“There is a poor prognosis for NSCLC patients without targetable alterations whose disease has progressed on platinum-based therapies and immune checkpoint inhibitors. Over 60% of patients progress on PD-1/PD-L1 inhibitors in NSCLC⁴. Unfortunately, multiple high-profile phase 3 studies failed to show overall survival benefit in this hard-to-treat population compared to standard of care docetaxel, a drug approved over 20 years ago. The data from the DUBLIN-3 Study demonstrates that the addition and proper sequencing of Plinabulin to docetaxel has a favorable benefit/risk ratio compared with docetaxel alone and may have broad utility. In addition, current ongoing 303 and 302 Studies are targeting additional severe unmet medical needs, which Plinabulin’s mechanism of action can help address.”

“With this capital, BeyondSpring is strategically positioned to advance our 303 and 302 studies in Plinabulin combination with immune checkpoint inhibitors to registrational trials and explore business development partnerships to bring Plinabulin to cancer patients with limited treatment options,” said **Dr. Lan Huang, Co-Founder, Chairman, and CEO of BeyondSpring**. *“At the same time, retaining a substantial stake in SEED Therapeutics ensures that we remain part of its continued success in revolutionizing drug discovery.”*

This press release shall not constitute an offer to sell or a solicitation of an offer to buy, nor shall there be any sale of these securities in any state or jurisdiction in which such an offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

Reference

1. La Sala G et al. Structure, Thermodynamics, and Kinetics of Plinabulin Binding to Two Tubulin Isotypes. *Chem* **5**: 1-18 (2019).
2. Kashyap AS et al. GEF-H1 Signaling upon Microtubule Destabilization Is Required for Dendritic Cell Activation and Specific Anti-tumor Responses. *Cell Rep* **28**(13): 3367-80 e8 (2019).
3. Han B. et al. Plinabulin plus docetaxel versus docetaxel in patients with non-small-cell lung cancer after disease progression on platinum-based regimen (DUBLIN-3): a phase 3, international, multicenter, single-blind, parallel group, randomized controlled trial. *Lancet Respir Med* **12**(10): 775-786 (2024).
4. Memon D. et al. Clinical and molecular features of acquired resistance to immunotherapy in non-small cell lung cancer. *Cancer Cell* **42**, 209-224 (2024).

About Plinabulin

Plinabulin is a novel first-in-class dendritic cell maturation agent with durable anti-cancer benefit observed across multiple clinical studies. As a reversible binder at a distinct tubulin pocket, Plinabulin does not change tubulin dynamics or antagonize tubulin stabilizing agents, such as docetaxel, which contributes to its differentiated activity and tolerability compared to other tubulin binders. In addition, Plinabulin significantly reduces chemotherapy induced neutropenia and could thereby increase docetaxel tolerability. Over 700 patients have been treated with Plinabulin with good tolerability.

About DUBLIN-3 (103) Study

DUBLIN-3 is a multicenter, single-blinded (patient) and randomized, phase 3 trial in 58 medical centers (US, China, and Australia, n=549). Only patients with EGFR wild-type NSCLC who had progressed after first-line platinum-based therapy were enrolled. Patients were randomized (1:1) to receive docetaxel (75 mg/m²) on Day 1 and either Plinabulin (30 mg/m²) or placebo on Days 1 and 8

in 21-day cycles until progression, unacceptable toxicity, withdrawal, or death. Treated patients were included in the safety analysis and ITT population in the primary efficacy analyses (NCT02504489). The primary endpoint for the study was OS, and secondary endpoints were PFS, ORR, Duration of Response (DoR), Grade 4 neutropenia and Quality of Life.

About 303 Study

303 Study is an open-label, single-arm Phase 2 Study of Plinabulin plus docetaxel and pembrolizumab for previously treated patients with metastatic NSCLC and progressive disease after anti-PD-(L)1 inhibitor alone or in combination with platinum-doublet chemotherapy. This study evaluates the efficacy and safety of this triple combination and is being conducted at Peking Union Medical College Hospital, Beijing, China. The regimen includes Pembrolizumab 200 mg IV every 3 weeks (Q3W) on Day 1, Docetaxel 75 mg/m² IV Q3W on Day 1 and Plinabulin 30mg/m² IV Q3W on Day 1 in a 21-day cycle. The primary endpoint is investigator-based ORR (RECIST 1.1). The secondary endpoints include PFS, OS, DoR, and safety. The study intends to enroll 47 patients. The study is funded by Merck's Investigator Studies Program with provision of study drug and financial support.

About 302 Study

302 Study is an open-label, single-arm Phase 2 Study of Plinabulin plus etoposide + platinum and pembrolizumab in first line extended-stage SCLC. This study evaluates the efficacy and safety of this combination and is being conducted at Wuhan Union Hospital in China, with Dr. Xiaorong Dong, Deputy Director of the Oncology Research Department and Director of the Thoracic Oncology Department, as the principal investigator. Patients enrolled are receiving the following interventional treatments for the first 4 cycles: Pembrolizumab 200 mg IV every 3 weeks (Q3W) on Day 1; Etoposide 100 mg/m² IV Q3W on Days 1, 2, and 3; Carboplatin AUC 5 IV Q3W on Day 1 or Cisplatin 75 mg/m² IV Q3W on Day 1; Plinabulin 30mg/m² IV Q3W on Day 1. From cycle 5, only Pembrolizumab and Plinabulin are given on Day 1 of each cycle. The primary endpoint is the 12-month PFS rate. The study intends to enroll 45 patients. The study is funded by Merck's Investigator Studies Program with provision of study drug and financial support.

About BeyondSpring

BeyondSpring is a global clinical-stage biopharmaceutical company developing innovative therapies to improve clinical outcomes for patients with high unmet medical needs. The Company is advancing its first-in-class lead asset, Plinabulin, into late-stage clinical development as a direct anti-cancer agent in NSCLC and a variety of cancer indications. Plinabulin binds to a differentiated pocket in tubulin, distinct from other tubulin binders, and is a potent inducer of dendritic cell maturation, which activates both adaptive and innate immunity. Plinabulin and docetaxel combination demonstrated significant overall survival benefit compared to docetaxel in second- and third-line NSCLC with EGFR wild type (Lancet Respir Med 2024). In addition, Plinabulin had been shown to significantly reduce severe neutropenia in a number of clinical studies. BeyondSpring's pipeline also includes three preclinical immuno-oncology assets. Learn more by visiting <https://beyondspringpharma.com>.

About SEED Therapeutics

SEED Therapeutics is an innovative biotech company focused on discovering and developing targeted protein degradation (TPD) therapeutics, with the mission to transform the treatment of diseases that currently have limited or no treatment options. Leveraging its cutting-edge RITE3[®] platform, SEED is at the forefront of molecular glue-based TPD, addressing diseases in oncology and neurodegeneration. Through active collaborations with Eli Lilly and Company and Eisai, and backed by a comprehensive intellectual property portfolio, SEED has built a robust pipeline of novel drug candidates that are now approaching clinical development. Learn more by

visiting www.seedtherapeutics.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this press release include, but are not limited to, statements regarding: the timing of the consummation of the proposed transactions; the anticipated benefits of the proposed transactions; the Company's anticipated progress, business plans, business strategy and clinical trials; the Company's advancement of its pipeline and its research, development and clinical capabilities; the Company's prioritization of its pipeline; and other statements that are not historical fact. These statements are based on the Company's current plans, objectives, estimates, expectations and intentions, are not guarantees of future performance and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, but are not limited to, risks and uncertainties related to: delays in or the inability to satisfy the conditions to complete the potential transactions; the inability to recognize the anticipated benefits of the potential transactions; business disruption during the pendency of or following the potential transactions; the effects of macroeconomic conditions, including any geopolitical instability and actual or perceived changes in interest rates and economic inflation; and other risks, including those described under the heading "Risk Factors" in the Company's Annual Report on Form 20-F for the year ended December 31, 2023, filed with the Securities and Exchange Commission on April 29, 2024. Forward-looking statements contained in this press release are made as of this date, and the Company undertakes no duty to update such information except as required under applicable law.

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