Press release

IBRILATAZAR (ABTL0812) from AbilityPharma increases chemotherapy effectiveness by 40% in patients with endometrial cancer

- **This is the key finding from the Phase 1/2 ENDOLUNG clinical trial, which was recently published in the prestigious scientific journal *BMC Cancer*.**
- **The trial evaluated the safety and efficacy of ibrilatazar (ABTL0812) combined with paclitaxel/carboplatin in 51 patients with advanced or recurrent endometrial cancer, across 9 leading oncology hospitals in Spain and France.**
- **Ibrilatazar is an oral drug with a novel mechanism of action that induces autophagy through the induction of ER-stress and the inhibition of the PI3K/Akt/mTOR pathway, which is crucial for cellular function and is implicated in this cancer type.**

Cerdanyola del Vallès (Barcelona, Spain), September 9, 2024. AbilityPharma, a clinical stage biopharmaceutical company specializing in the development of innovative oncology therapies, today announced that the final data of its Phase 1/2 ENDOLUNG trial evaluating ibrilatazar (ABTL0812) in combination with chemotherapy (paclitaxel/carboplatin) for patients with advanced or recurrent endometrial cancer has been published in *BMC Cancer*.

The trial benefited from the contribution of global key opinion leaders from select hospitals in Spain and France, including the Vall d'Hebron Institute of Oncology (VHIO) in Barcelona, Gustave Roussy in Paris, Clinic University Hospital in Valencia, Centre Léon Bérard in Lyon, Virgen del Rocío University Hospital in Seville, Paoli-Calmettes Institute in Marseille and the Catalan Institute of Oncology (ICO) in Badalona, l'Hospitalet and Girona.

This significant publication builds upon AbilityPharma's previous groundbreaking translational research, which was featured in *Gynecologic Oncology*. These advancements further establish the company's **leadership in the development of autophagy-mediated oncology drugs**.

Dr. Carles Domènech, AbilityPharma's CEO & Co-Founder, stated, "This publication represents a crucial development in the study of new drugs and combinations for advanced endometrial cancer, marking a significant milestone in AbilityPharma's mission to deliver transformative treatments to cancer patients".

The first author of the article is **Dr. Alexandra Leary**, deputy director of the Department of Clinical Oncology at Gustave Roussy, and the senior authors of the article, with equal contribution, are **Dr. Alejandro Pérez-Fidalgo**, oncologist at the Clinic University Hospital in Valencia, researcher at the

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INCLIVA Biomedical Research Institute's Oncology Department and member of the Biomedical Research Network in Cancer (CIBERONC), and **Dr. Ana Oaknin**, Group Leader of VHIO's Gynecological Malignancies Group and Head of Gynecologic Tumors Unit, Medical Oncology Department, at the Vall d'Hebron University Hospital.

"The PI3K pathway is almost universally altered in endomettial cancer and thus represents a very interesting target. Ibrilatazar is the first PI3K inhibitor demonstrating encouraging activity and excellent side effect profile in the capsule form now available", noted Dr. Alexandra Leary of Gustave Roussy.

Dr. Alejandro Pérez-Fidalgo of Clinic University Hospital in Valencia explains that, "ibrilatazar, when administered in combination with chemotherapy and subsequently as maintenance therapy, has shown a median survival of over 9 months in advanced endometrial cancer. These results are highly promising. If confirmed in a randomized study, ibrilatazar could become a treatment alternative for this complex disease."

Summary of main results reported in the publication

- The combination of ibrilatazar plus CP demonstrated an overall response rate (ORR) of 65.8%, comprising a 13.2% complete response and a 52.6% partial response, with a median duration of response (DOR) of 7.4 months (95% CI: 6.3–10.8 months). The median progression-free survival (PFS) was 9.8 months (95% CI: 6.6–10.6), **a 40% increase over historical controls**, with event-free rates of 73.3% at 6 months and 24.4% at 1 year. The median overall survival (OS) was 23.6 months (95% CI 6.4-ND), with an event-free rate of 74.9% at 1 year. These results suggest an increased efficacy over reference historical controls where ORR, PFS and OS were 51%, 7.1 months and 20.4 months.
- The combination of ibrilatazar plus paclitaxel/carboplatin exhibited a good safety profile. ibrilatazar aligned with the safety profile of historical controls and did not introduce additional significant adverse events beyond those associated with CP.
- Pharmacokinetic parameters aligned with target engagement observed in preclinical trials, and blood pharmacodynamic biomarkers indicated sustained target regulation for at least 28 days following the initiation of treatment.

Reference article: *ENDOLUNG trial. A phase 1/2 study of the Akt/mTOR inhibitor and autophagy inducer ibrilatazar (ABTL0812) in combination with paclitaxel/carboplatin in patients with advanced/recurrent endometrial cancer*

About endometrial cancer

Endometrial cancer is the sixth most common cancer among women worldwide, with over 400,000 new cases diagnosed each year. The incidence of this disease has risen globally by 132% over the

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past 30 years and is expected to continue to increase due to an aging population and rising global rates of obesity and diabetes. More than 90% of cases occur in women over 50 years of age. In developed countries, it is the most prevalent gynecological cancer.

About ibrilatazar (ABTL0812)

Ibrilatazar is a first-in-class, fully differentiated oral targeted anticancer compound that induces cell death selectively in cancer cells (and not in normal cells) through autophagy (self-digestion). The mechanism of action of ibrilatazar is both unique and novel. The robust autophagy comes from the combined induction of PPAR-dependent endoplasmic reticulum stress (ER stress) and the inhibition of Akt activation, the central kinase in the PI3K/Akt/mTOR pathway. The mechanism of action was published in *Clinical Cancer Research* (2016) and in *Autophagy* (2020).

In clinical trials, ibrilatazar showed clinical benefit for patients with endometrial and lung cancer. Also, it showed robust preclinical proof-of-concept in animal models of cancer types, including lung, endometrial and pancreatic cancer, neuroblastoma, and glioblastoma.

AbilityPharma is currently evaluating ibrilatazar in metastatic pancreatic cancer through a Phase 2b PanC-ASAP clinical trial with 140 patients in USA, Spain, France and Israel. Recruitment was completed in January 2024 and an efficacy interim analysis was successfully passed on April 2024.

Ibrilatazar received Orphan Drug Designations (ODD) for pancreatic cancer, biliary cancer, and the pediatric cancer neuroblastoma by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

About AbilityPharma

AbilityPharma is a clinical-stage biopharmaceutical company developing innovative cancer treatments, with a focus on autophagy as a new therapeutic strategy to induce selective death of cancer cells. Its main drug, ibrilatazar (ABTL0812), is in development for pancreatic cancer (ongoing Phase 2b), lung cancer (Phase 2a) and endometrial cancer (Phase 1/2).

In 2016, AbilityPharma signed a licensing agreement with SciClone Pharmaceuticals to develop and market ibrilatazar in China. Current shareholders include CTI Life Sciences Fund, Inveready, EIC Fund, FiTalent, CDTI Innvierte, SODENA, SciClone Pharmaceuticals, its founders and private investors. The company also receives financial support from the European Commission, the Ministry of Science and Innovation (Government of Spain), the Center for the Development of Industrial Technology (CDTI), the Official Credit Institute (ICO), ENISA and ACCIÓ (Government of Catalonia). The company is headquartered in the Parc Tecnològic del Vallès (Cerdanyola del Vallès, Barcelona).

More information: www.abilitypharma.com

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