

ADC Therapeutics Announces First Patient Dosed in Phase I Clinical Trial of ADCT-402 (loncastuximab tesirine) and Ibrutinib in Patients with Advanced Diffuse Large B-Cell Lymphoma or Mantle Cell Lymphoma

Combination trial to evaluate safety and anti-tumor activity of agents that target B-cell cancers

Lausanne, Switzerland, February 20, 2019 – ADC Therapeutics, an oncology drug discovery and development company that specializes in the development of proprietary antibody drug conjugates (ADCs), today announced that the first patient has been dosed in a Phase I clinical trial evaluating the safety, tolerability, pharmacokinetics and anti-tumor activity of ADCT-402 (loncastuximab tesirine) in combination with Pharmacyclics LLC’s ibrutinib in patients with advanced diffuse large B-cell lymphoma (DLBCL) or mantle cell lymphoma (MCL).

ADCT-402, an ADC designed to target and kill CD19-expressing malignant B-cells, is also being evaluated in an ongoing pivotal Phase II clinical trial in patients with relapsed or refractory (R/R) DLBCL and a Phase I clinical trial in combination with IMFINZI® (durvalumab) in patients with multiple types of R/R non-Hodgkin lymphoma. Ibrutinib, a small-molecule inhibitor of Bruton’s tyrosine kinase that is jointly developed and commercialized by Pharmacyclics LLC, an AbbVie company, and Janssen Biotech, Inc., is a mediator of the B-cell-receptor signaling pathway implicated in the pathogenesis of B-cell cancers. Ibrutinib is approved for use in patients with R/R MCL and has shown some activity in R/R DLBCL.

Jay Feingold, MD, PhD, Chief Medical Officer and Senior Vice President of Clinical Development at ADC Therapeutics, said, “At the 60th American Society of Hematology (ASH) Annual Meeting, the data we presented from our 183-patient first-in-human clinical trial of ADCT-402 demonstrated its encouraging safety profile and anti-tumor activity as a single agent against relapsed or refractory diffuse large B-cell lymphoma and mantle cell lymphoma. Now, in our second combination trial of ADCT-402, we look forward to exploring whether ADCT-402 and ibrutinib, both of which target B-cell cancers with different mechanisms of action, may increase the response rate and durability of response compared to the effects of these compounds as single agents.”

Julien Depaus, MD, an investigator for the trial at CHU UCL Namur, Yvoir, Belgium, said, “Unfortunately, a significant number of patients with B-cell malignancies will relapse after initial treatment. As the prognosis for these patients is poor, it is important to evaluate potential viable new treatments for relapsed or refractory diffuse large B-cell lymphoma and mantle cell lymphoma, such as the combination of ADCT-402 and ibrutinib we are studying in this Phase I trial.”

The open-label, single-arm trial will include a dose-escalation part, followed by a dose-expansion part. The dose-expansion part may have up to two cohorts, one for DLBCL and one for MCL, in order to obtain additional safety and preliminary anti-tumor activity information at the maximum tolerated dose. Approximately 60 patients will be enrolled in the trial. For more information, please visit www.clinicaltrials.gov (identifier NCT03684694).

ADCT-402 Interim First-in-Human Data

Updated data from the ongoing 183-patient Phase I clinical trial of ADCT-402 were presented at the 60th American Society of Hematology (ASH) Annual Meeting. In a subpopulation of 139 evaluable patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) who had failed or were intolerant to established therapies, ADCT-402 demonstrated manageable toxicity. At doses >120 µg/kg, the overall response rate (ORR) was 43.3 percent (55/127 patients with DLBCL), comprising 23.6 percent complete responses and 19.7 percent partial responses. In a subgroup of 15 patients with mantle cell lymphoma (MCL), ADCT-402 demonstrated manageable toxicity, and ORR was 46.7 percent (7/15) and median duration of response was not reached after a median follow-up time of 8.7 months.

About ADCT-402

ADCT-402 (loncastuximab tesirine) is an antibody drug conjugate (ADC) composed of a humanized monoclonal antibody that binds to human CD19, conjugated through a linker to a pyrrolobenzodiazepine (PBD) dimer toxin. Once bound to a CD19-expressing cell, ADCT-402 is internalized into the cell where enzymes release the PBD-based warhead. CD19 is a clinically validated target for the treatment of B-cell malignancies. The PBD-based warhead has the ability to form highly cytotoxic DNA interstrand cross-links, blocking cell division and resulting in cell death. ADCT-402 is being evaluated in a pivotal Phase II clinical trial in patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) ([NCT03589469](https://clinicaltrials.gov/ct2/show/study/NCT03589469)), a Phase I clinical trial in combination with IMFINZI® (durvalumab) in patients with R/R DLBCL, mantle cell lymphoma or follicular lymphoma ([NCT03685344](https://clinicaltrials.gov/ct2/show/study/NCT03685344)) and a Phase I clinical trial in combination with ibrutinib in patients with R/R DLBCL or mantle cell lymphoma ([NCT03684694](https://clinicaltrials.gov/ct2/show/study/NCT03684694)). The U.S. Food and Drug Administration granted orphan drug designation to ADCT-402 for the treatment of DLBCL and MCL.

About ADC Therapeutics

ADC Therapeutics SA is an oncology drug discovery and development company that specializes in the development of proprietary antibody drug conjugates (ADCs) targeting major hematological malignancies and solid tumors. The Company's ADCs are highly targeted biopharmaceutical drugs that combine monoclonal antibodies specific to surface antigens present on particular tumor cells with a novel class of highly potent pyrrolobenzodiazepine (PBD)-based warheads via a chemical linker. The Company has five PBD-based ADCs in ongoing clinical trials, ranging from first in human to pivotal Phase II, in the USA and Europe, and a deep pipeline of other preclinical ADCs in development. ADC Therapeutics has world-class partners, including AstraZeneca and its global biologics research and development arm, MedImmune. The Company is based in Lausanne (Biopôle), Switzerland and has operations in London, San Francisco and New Jersey. For more information, visit www.adctherapeutics.com.

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