



## **Cleave Biosciences Initiates Phase 1 Clinical Trial of CB-5083 in Patients with Multiple Myeloma**

**Burlingame, Calif. – September 4, 2014** – Cleave Biosciences today announced that it has begun a Phase 1 clinical trial to evaluate its lead drug candidate, CB-5083, in patients with relapsed and refractory multiple myeloma. CB-5083 is a first-in-class, oral inhibitor of p97, a critical enzyme that controls various aspects of protein homeostasis.

The open-label, Phase 1 dose escalation/dose expansion trial will evaluate the safety, pharmacokinetics, pharmacodynamics and anti-tumor activity of CB-5083 in multiple myeloma patients who have relapsed/refractory or refractory disease after receiving two or more lines of therapy, including an immunomodulatory agent (IMiD) and a proteasome inhibitor. Cleave expects to enroll up to 60 patients at multiple U.S. cancer centers that are part of the Multiple Myeloma Research Consortium. More information about the trial, including enrolling centers, is available by visiting [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (ID # NCT02223598) or [www.cleavebio.com](http://www.cleavebio.com).

“Patients with multiple myeloma whose disease is resistant to existing therapies have run out of options. We are eager to assess CB-5083 in this trial and to further understand which tumors are dependent on the p97 pathway for their growth and survival so we can focus our future clinical program on the patients most likely to benefit from this potential treatment,” said Laura Shawver, Ph.D., Chief Executive Officer of Cleave Biosciences.

Cleave Biosciences discovered CB-5083 through a targeted screening and medicinal chemistry effort. CB-5083 is a potent, specific and orally bioavailable inhibitor of p97 for which anti-tumor activity has been characterized *in vivo* in tumor-bearing mice. It has robust activity in multiple hematological models as well as in solid tumor xenograft models that are resistant to proteasome inhibitors. Pharmacologic interference with p97 function in tumors generates irresolvable endoplasmic reticulum stress that induces a lethal unfolded protein response, which in turn leads to apoptosis and profound antitumor activity.

“Targeting protein homeostasis is a well-established approach for the treatment of patients with multiple myeloma, but eventually many patients relapse or no longer respond to therapy. By disrupting protein homeostasis using a completely novel target, we hope to validate CB-5083’s mechanism and establish its path forward for patients with myeloma,” said Sagar Lonial, M.D., Director of Translational Research, B-cell Malignancy Program and Professor of Hematology and Medical Oncology at the Winship Cancer Institute of Emory University.

Preclinical studies also demonstrate significant promise for CB-5083 in solid tumors. Cleave is currently planning to initiate a Phase 1 trial in solid tumors later this year.



CB-5083 is derived from a compound initially synthesized by the Specialized Chemistry Center at the University of Kansas, which is part of the National Institutes of Health's Molecular Libraries Program. Cleave's discovery partners also include Tsui-Fen Chou, Ph.D. from the laboratory of Raymond J. Deshaies, Ph.D., who is Professor of Biology, California Institute of Technology, a Howard Hughes Medical Institute Investigator and a Scientific Founder of Cleave Biosciences; and The Scripps Research Institute, also a member of the Molecular Libraries Program.

### **About Multiple Myeloma**

Multiple myeloma, also known as myeloma, is a hematologic cancer, or cancer of the blood, that develops in the plasma cells in bone marrow. It is the second most common blood cancer, after non-Hodgkin's lymphoma. The National Cancer Institute estimates that in the U.S., approximately 70,000 people are living with multiple myeloma and approximately 24,050 new cases will be diagnosed this year. Worldwide, nearly 230,000 people are living with the disease and approximately 114,000 new cases are diagnosed annually.

### **About Cleave Biosciences**

Biopharmaceutical company Cleave Biosciences is a pioneer in the discovery and development of drugs that target protein homeostasis systems and have the potential to transform the treatment of people with difficult to treat solid tumors and hematologic malignancies. The company is privately held and located in Burlingame, California. For additional information, visit [www.cleavebio.com](http://www.cleavebio.com).

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