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Forbius' AVID200 IND Receives Clearance from the FDA to Start Phase 1 Scleroderma Clinical Trial

August 24, 2018 – Forbius announced today that the U.S. Food and Drug Administration (FDA) has cleared its investigational new drug (IND) application for AVID200, an isoform-selective TGF-β inhibitor. This enables the company to begin a Phase 1 clinical study to evaluate AVID200 as a potential treatment for diffuse cutaneous systemic sclerosis (SSc), a life-threatening fibrotic disease.

SSc is a rare, severe, and progressively debilitating fibrotic disease, affecting predominately women in mid-life. The 10-year survival rate of SSc patients is approximately 55%. No therapeutic is currently approved for the treatment of SSc, which affects an estimated 50,000 people in the U.S. alone.

TGF-β is now widely accepted as being the primary driver of SSc pathogenesis (Lafyatis, R. *Nat. Rev. Rheumatol.* 10, 706–719 (2014)). Gene expression data demonstrate the increased expression of TGF-β regulated genes in SSc skin. Moreover, the extent of upregulation of expression of two of the three TGF-β isoforms (-β1 & -β3), which are the isoforms blocked by AVID200, correlates with the severity of SSc (O'Connor *et al*, JSRD, 2018, CO.22 Vol 3(15):22-25)

"I am keen to investigate the potential of AVID200 to reverse this life-threatening condition. A substantial body of preclinical and clinical data demonstrate that the basic defect in SSc is diffusely increased TGF-β activity and that inhibition of TGF-β could reverse this disease. AVID200 appears to have the right profile to be the first disease modifying agent in SSc," commented Coordinating Principal Investigator, Robert Lafyatis, M.D., Professor of Medicine, Medsger Professor and Director of the University of Pittsburgh Scleroderma Center at the University of Pittsburgh Medical Center.

The Phase 1 dose-escalation study will be conducted in multiple study centers throughout the United States. The trial will evaluate safety and pharmacokinetics, as well as pharmacodynamics and preliminary evidence of efficacy of AVID200 as a potential treatment of SSc.

About AVID200
The AVID200 program was recently featured in an oral presentation at the 5th Systemic Sclerosis World Congress and received an award from the World Scleroderma Foundation as "One of the Most Original Works Presented at the Congress".

AVID200 is designed to be a highly potent and isoform-selective TGF-β inhibitor. AVID200 is unique since it selectively neutralizes TGF-β1 and -β3 with pM potency, while at the same time being minimally active against TGF-β2. Inhibiting the TGF-β1 and -β3 isoforms is advantageous since overexpression of these isoforms is closely associated with the progression of fibrosis and cancer. Conversely, blockage of TGF-β2 is undesirable because of the potential impact on normal cardiac function and dissemination of metastasis. AVID200 is therefore positioned to be an effective and well-tolerated therapeutic in a variety of clinical settings. AVID200 is undergoing development for

info@forbius.com
forbius.com

the treatment of fibrotic diseases and immune oncology.

About Forbius (Formation Biologics)
Forbius is a clinical stage company that designs and develops biotherapeutics for the treatment of cancer and fibrotic diseases. Forbius' medicines are designed to radically transform patients' lives. We use our strength in biological understanding and diverse protein engineering technologies to design superior inhibitors of validated pathways.

We have particularly deep expertise in targeting the transforming growth factor-beta (TGF-β) and epidermal growth factor receptor (EGFR) pathways. For both of these pathways, there is a significant body of evidence validating their role as drivers of multiple life-threatening conditions, including cancer and fibrosis. However, in the case of the EGFR pathway, the majority of patients do not benefit from currently marketed EGFR inhibitors; in the case of the TGF-β pathway, no agent targeting this pathway has yet been approved. By using multiple complementary platform technologies, Forbius' team overcame barriers that prevented the development of effective therapeutics targeting these pathways. For more information, please visit www.forbius.com.

info@forbius.com
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