

## **Ensemble Therapeutics Presents Oral Efficacy of First-in-Class Small Molecule Targeting IL-17 for Inflammation in Preclinical Studies**

*Oral Activity of Novel Small Molecule Interleukin-17 Antagonists in Multiple Models of Inflammation Presented at the 2012 ACR Annual Meeting*

*On Track to Select Orally Active IL-17 Drug Candidate in early 2013*

CAMBRIDGE, MA – November 12, 2012 -- Ensemble Therapeutics, a biotechnology company developing Ensemblins™, a novel class of small molecule therapeutics with the power of biologics, announced today positive preclinical oral efficacy data with its first-in-class small molecule Interleukin-17 (IL-17) antagonists. A presentation at the American College of Rheumatology (ACR) 2012 Annual Meeting, taking place November 9-14, 2012 in Washington, DC, revealed that the company's Ensemblins have strong oral activity as antagonists of IL-17, a pro-inflammatory cytokine implicated in multiple inflammatory and autoimmune diseases such as psoriasis, rheumatoid arthritis, Crohn's disease and inflammatory bowel disease.

"We have made dramatic progress since the first announcement of our small molecule IL-17 antagonist program earlier this year." said Dr. Michael D. Taylor, CEO of Ensemble Therapeutics. "This data is compelling in showing excellent oral efficacy in vivo for several lead molecules, which puts us solidly on track to nominate an oral drug candidate for clinical development early in 2013."

The Ensemblins studied represent first-in-class, orally active, small molecule antagonists of the important, clinically validated protein-protein-interaction target, IL-17, that has proven impervious to traditional small molecule pharmaceutical approaches and has only been addressed to date with injectable protein therapeutics. A small orally active inhibitor of IL-17 would have significant advantages over the current class of clinical stage anti-IL-17 antibody products which cannot be administered orally.

In a poster presentation entitled "Identification and Characterization of Synthetic Small Molecule Macrocyclic Antagonists of Human IL17A", Dr. David J. Livingston, Ensemble SVP Biology, presented preclinical data on oral anti-IL-17A Ensemblins, including:

- *High selectivity to the cytokine target*
  - The anti-IL-17A Ensemblins bind to IL-17A and specifically inhibit IL-17A induction of cytokines and chemokines in cell assays. In addition, they demonstrate selectivity for IL-17 induced cellular responses compared to responses induced by other pro-inflammatory cytokines.
- *Comparable anti-inflammatory efficacy to an anti-IL-17 antibody*
  - *The anti-IL-17A antagonist referred to as E-36041 was shown to be orally active in a murine collagen-induced arthritis (CIA) model, displaying similar protection from inflammation as an anti- mouse IL-17A antibody.*
- *Protection from arthritic joint degradation*

- E-36041 suppressed arthritis disease-induced changes in joints such as pannus formation and bone resorption and remodeling.
- *Significant in Vivo Activity*
  - The IL-17A inhibitors were active in vivo in murine models of acute inflammation when injected intraperitoneally (into the body cavity) or by oral gavage (feeding tube).

“These data demonstrated Ensemble’s ability to rapidly identify and optimize the properties of these compounds for oral activity while maintaining outstanding potency and selectivity,” said Dr. Nick Terrett, CSO of Ensemble. “This achievement is a highly encouraging demonstration of our macrocycle drug discovery platform to address difficult drug targets such as protein-protein interactions.”

Ensemble’s proprietary IL-17 program is an internal macrocycle drug development effort within the company’s therapeutic focus areas of oncology and immuno-inflammatory diseases. Concurrently the company is advancing other drug programs on behalf of its partners.

## **About Ensemblins**

Ensemblins™ are a new class of synthetic macrocycles developed by Ensemble using its proprietary chemistry platforms, including DNA-Programmed Chemistry. Macrocyclic rings are found in many natural product-based drugs and bestow favorable pharmaceutical properties and powerful protein surface binding properties upon such drugs. Thus, macrocycles are uniquely suited to address many protein targets that cannot be modulated effectively by traditional small molecule pharmaceutical compounds. Macrocycles have been challenging to synthesize in large numbers and this has constrained their wider use in the industry. By extending beyond the limits of traditional small molecule drug discovery, Ensemble’s platform provides unmatched capabilities to successfully and reliably generate millions of macrocyclic Ensemblins as drug candidates, larger than any collection previously synthesized in the pharmaceutical industry.

## **About Ensemble Therapeutics Corporation**

Based in Cambridge, MA, Ensemble Therapeutics is deploying its proprietary chemistry platforms to develop a novel class of therapeutics known as “Ensemblins”. Ensemble is leveraging its macrocyclic drug discovery expertise to fuel its proprietary drug candidate pipeline while also pursuing collaborations with pharmaceutical partners. Ensemble has established high-value partnerships including alliances with Boehringer Ingelheim, Genentech, Bristol-Myers Squibb and Pfizer. Ensemble develops Ensemblins against pharmaceutical targets for which a strong therapeutic rationale exists but which have not been previously or optimally addressed with traditional small molecules. Although some of those targets might be addressed with biologics, many opportunities remain unexploited either because a small molecule oral medication is a preferred route of administration or because the target is inaccessible to biologics. Ensemble’s internal discovery and development efforts are focused on the key therapeutic areas of oncology and immuno-inflammatory diseases, with its lead program, a small molecule antagonist of Interleukin-17, a cytokine implicated in multiple inflammatory and autoimmune diseases, poised to enter development with an orally active candidate in early 2013. For

# ENSEMBLE | THERAPEUTICS



more information, visit: [www.ensembletx.com](http://www.ensembletx.com).

Media Contact:

Gina Nugent  
The Yates Network  
617-460-3579