

A Revolution in Drug Discovery

Focus on the toughest drug discovery targets: **Protein-Protein Interactions**. Create a new class of compounds ideally suited to address those targets: **Ensemblins™ (synthetic macrocycles)**. Engineer those molecules in diverse collections totaling nearly 12 million macrocycles using a revolutionary chemistry platform: **DNA-Programmed Chemistry**. Combine the chemistry with a powerful, extremely efficient screening platform. Assemble a world-class medicinal chemistry capability that can rapidly synthesize and optimize macrocycles to nanomolar potency and oral efficacy. Execute productive partnerships with major pharma companies. Build a track record of success in delivering successful programs for our partners and our own proprietary portfolio. **That is the story of Ensemble Therapeutics.**

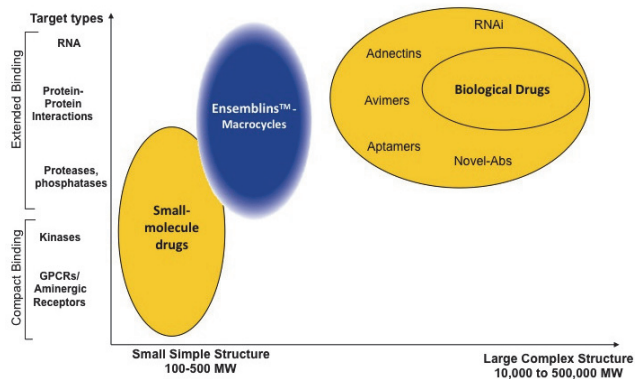
Benefits of Ensemblin Macrocycles

- **Distinct Pharmaceutical Properties:** Provides oral bioavailability, cell penetration, metabolic stability and readily scalable synthesis.
- **Target affinity and selectivity:** Inhibits protein targets not addressed by small molecules (PPIs, proteases, etc.)
- **Versatility:** Inhibits targets across multiple disease areas (inflammation, immune disorders, cancer, etc.)

Small Molecules with the Power of Biologics™

Ensemblins are a new class of drugs in an emerging therapeutic space between small molecules and biologics capable of addressing historically challenging disease targets. With their distinctive macrocyclic ring structure, Ensemblins have unique chemical and biological properties designed to achieve uncommonly high levels of affinity and specificity. Ensemblins go beyond the limits of traditional small molecules through their potential to bind to targets (e.g., PPIs) that are only addressable today with biologics, yet retain small molecule drug qualities such as oral bioavailability and intracellular permeability.

Ensemblins™: Occupying an emerging therapeutic space between small molecules and biologics



Ensemble Pipeline

Ensemble is focusing its proprietary discovery and development efforts in the key therapeutic areas of oncology and immuno-inflammatory diseases. In addition to its own programs, Ensemble has made substantial and rapid progress together with its collaboration partners against a number of high-value drug targets in multiple therapeutic areas.

Discovery	Optimization	Preclinical
IL-17A Antagonists – Autoimmune <i>Alliance initiated August 2013</i>		NOVARTIS
Intracellular, Dual-Target Program <i>Hand-off 2011</i>		Bristol-Myers Squibb
Discovery Programs <i>Initiated May 2012</i>	Genentech <small>A Member of the Roche Group</small>	
Discovery Programs <i>Initiated Oct. 2012</i>	Boehringer Ingelheim	
Discovery Programs <i>Initiated July 2013</i>	ALEXION	
Discovery Programs <i>Initiated August 2013</i>	NOVARTIS	
Multiple In-House Programs <i>Oncology and Inflammation focus</i>	ENSEMBLE THERAPEUTICS	

Oral Small Molecule Antagonists of Interleukin-17

Ensemble identified a proprietary series of first-in-class, orally bioavailable, small molecule antagonists of Interleukin-17, an important pro-inflammatory cytokine implicated in multiple inflammatory and autoimmune diseases, a program which Ensemble partnered with Novartis in a development collaboration in August 2013. IL-17 is a clinically validated Protein-Protein Interaction target that has proven impervious to traditional small molecule pharmaceutical approaches and has only been addressed to date with protein therapeutics. A small orally-active inhibitor of IL-17 would have significant delivery and therapeutic advantages over current clinical stage anti-IL-17 antibody products. Ensemble presented positive oral efficacy data of prototype Ensemblin IL-17 inhibitors in DTH and CIA murine models of inflammation at the American College of Rheumatology (ACR) 2012 annual meeting. Ensemble expects that its collaboration with Novartis will produce an orally active development candidate in due course.

Delivering Successful Programs for Partners Against Intractable Protein Targets

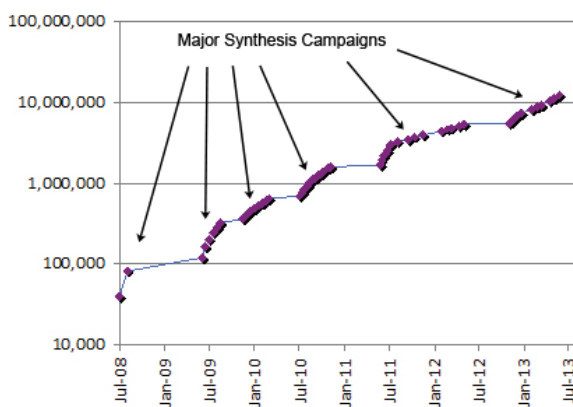
In August 2013, Ensemble announced the formation of a two-part research and development alliance with **Novartis** for the advancement of Ensemble's proprietary oral small molecule program targeting the inflammatory cytokine IL-17 and for the discovery of novel small molecule treatments against additional undisclosed drug targets specified by Novartis using Ensemble's proprietary drug discovery platforms.

In July 2013, Ensemble announced the initiation of a drug discovery collaboration with **Alexion Pharmaceuticals**, adding to Ensemble's collaborator roster that includes **Boehringer Ingelheim** (a \$186 million alliance formed in 2012), **Genentech** (also formed in 2012), **Pfizer** (2010) and **Bristol-Myers Squibb** (2009), for the discovery and development of Ensemblins against certain exclusive high-value Protein-Protein Interaction targets. For these alliances, Ensemble receives license fees and research funding, plus future preclinical and clinical milestones and royalties on sales of products successfully advanced and commercialized by our collaborators.

Ensemble has discovered validated new chemistry for several previously intractable targets for our partners. In April 2011, Ensemble successfully delivered a completed program directed at an intracellular PPI target for which BMS paid Ensemble a hand-off milestone and is now advancing thru candidate nomination steps.

Ensemblin Product Platform: DNA-Programmed Chemistry (DPC™)

Ensemble extends the limits of traditional small molecule drug discovery through its DNA-Programmed Chemistry™ (DPC) platform. DPC gives the company unmatched capabilities to successfully and reliably generate millions of synthetic macrocyclic Ensemblins™ as drug candidates. Ensemble screens its macrocyclic compounds for biological activity against many high-value targets through a rapid, highly sensitive and efficient affinity selection process to successfully generate leads. Ensemble has built a library of about 12 million macrocyclic Ensemblins, the largest set of such compounds ever assembled in the pharmaceutical industry.



Macrocycle diversity expanded in each additional synthesis campaign

Unparalleled Productivity for Discovery

Speed: 3-month cycle

- Millions of compounds screened.
- Hits and SAR revealed through bioinformatics of DNA "bar codes."
- Hits synthesized (free of DNA) for biochemical validation.

Efficiency

- Economical screening process; next generation DNA sequencing; low FTE requirements.

Results

- Discovery of unique chemical matter starting points for multiple "undruggable" targets.
- Thousands of macrocycles scaled up to optimize potency, selectivity and pharmacokinetics by Ensemble's medicinal chemists.

Company Background

Ensemble has assembled an experienced management team and a strong set of investors, including Flagship Ventures, ARCH Venture Partners, CMEA, Harris & Harris, Kisco Ltd. and Boston University. Ensemble has raised \$38.5 million of equity financing to date.

Ensemble's extensive patent estate includes an exclusive, worldwide license from Harvard University to Prof. David Liu's powerful DNA-Programmed Chemistry platform.

Management Team

Stephen Hale, Ph.D.

SVP Biological Sciences,
formerly Praecis

Ted Hibben, MBA

SVP Corporate Development,
formerly Cequent, Coley

John Ripple, MBA

CEO, formerly Virdante,
Syntonix, Wyeth

Andrea Szekely-Hill, CPA

Senior Director Finance and
Administration, formerly Deloitte

Nicholas Terrett, Ph.D.

CSO, formerly Pfizer R&D

Board of Directors

Noubar Afeyan (Chairman)

Managing Partner,
Flagship Ventures

Douglas Cole

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