

Invenra, Inc.

www.invenra.com



## Expanding the search for therapeutic antibodies

Invenra's new proprietary platform, which combines cell-free protein expression with extreme miniaturization, enables the direct phenotypic interrogation of large numbers of full-length antibodies and their derivatives, empowering the discovery of next-generation biologics.

Invenra is bringing microarray technology and miniaturization to the discovery of therapeutic monoclonal antibodies (mAbs) and their derivatives. Invenra's proprietary technology is a fusion of ribosome display, microarrays, cell-free expression of full-length antibodies, and cell-based assays carried out in the company's nanowell arrays. This combination of technologies gives Invenra a powerful platform for discovering the next generation of therapeutic antibodies and antibody derivatives.

Founded in 2011 and based in Madison, Wisconsin, the privately funded company has its roots in the world of DNA technology. CEO and co-founder Roland Green previously co-founded the DNA microarray company NimbleGen Systems, where he served as CTO and VP of R&D until NimbleGen's acquisition by Roche for \$272.5 million in 2007. Green continued in-house at Roche, where he was introduced to next-generation sequencing and the drug-discovery side of the business.

Invenra's proprietary technology is based on the production of full-length antibodies via cell-free expression using an *in vitro* biochemical protein-synthesis system. An *Escherichia coli* cell extract is mixed with template DNA of the desired protein, plus other necessary building blocks such as amino acids and nucleotides. The system generates high titers (up to 400  $\mu\text{g ml}^{-1}$ ) of full-length, fully folded and functional antibodies in under 6 h.

Invenra's cell-free synthesis system has produced numerous antibodies that are structurally comparable to those produced by other systems. They bind with high specificity and have similar binding affinities. According to Green, "We are leveraging the tools of the DNA world to meet the challenges of antibody discovery."

### Antibody fast track

What really sets Invenra apart is the company's ability to move from a ribosome-display library enriched for target binders to cell-phenotype data on hundreds of thousands of full-length antibody candidates in a matter of days.

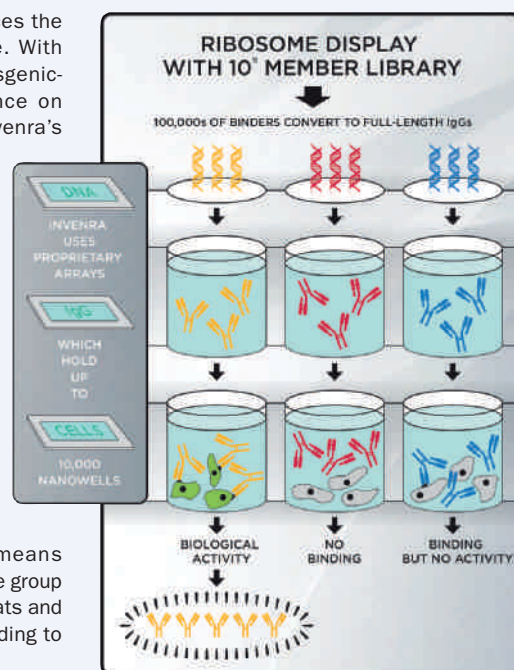
"Our precision-engineering capabilities allow us to synthesize, purify and release antibodies into corresponding nanowells containing cells, and perform hundreds of thousands of immunotypic or more biologically relevant assays," said Invenra's head of R&D, Bryan Glaser. Rather than just looking at antibody affinity, Invenra is able to directly interrogate phenotype and resulting biological activity, leading to the selection of the best lead compounds.

Invenra's screening platform produces the broadest epitope coverage possible. With traditional murine hybridoma or transgenic-animal approaches, there is reliance on the animal's immune system, but Invenra's *in vitro* approach allows for the production of mAbs targeting non-immunodominant epitopes. "We can create mAbs that are not governed by the immunodominance of any one epitope on a given target protein," said Green.

The Invenra platform is compatible with most modern protein-engineering formats—the company calls it 'scaffold agnostic'. Because the process starts with DNA, molecules can be designed *de novo* in any format, including full-length antibodies, bispecific molecules and antibody-drug conjugate molecules, which means Invenra is "able to partner with a diverse group of companies, given the variety of formats and applications we can work with," according to Green.

Invenra Director Rick Lesniewski is convinced that the company's platform has great potential. A former director of cancer research at Abbott Laboratories and VP of oncology biopharmaceuticals at GlaxoSmithKline, Lesniewski said, "My discovery teams would have benefited greatly from this technology. The ability to secure significant numbers of biological drug hits of known sequence, from a high-diversity human DNA library all having a predetermined cellular phenotype, on these timelines, is a high-value proposition to biologics discovery programs." The versatile Invenra approach could also be useful for drugs targeting G-protein-coupled receptors and ion channels, as the ability to go straight to phenotypic screening and functional activity is a big advantage.

Invenra is interested in collaborating with early-access partners under flexible financial terms. The company is involved in ongoing discussions with a number of potential partners focused on applications where Invenra's technology provides a potential best-in-class solution. Invenra is also developing its own proprietary product pipeline, with a focus on immuno-oncology, using its unique platform to provide a quick and cost-effective route to high-caliber lead therapeutics.



**Figure 1: Invenra's therapeutic antibody discovery technology.** Invenra converts hundreds of thousands of binders from ribosome display into full-length antibodies or derivatives, such as bispecifics and antibody-drug conjugates, for direct phenotypic screening, while maintaining genotypic linkage. A DNA array acts as a template for the production of an antibody-dosing array using Invenra's cell-free expression system. Next, antibodies are released into cell-containing nanowells to identify the most biologically relevant therapeutic candidates.

### CONTACT DETAILS

**Mark F. Kubik**, VP, Business Development  
Invenra, Inc.  
Madison, Wisconsin, USA  
Tel: + 1-608-284-1766  
Email: mkubik@invenra.com