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VP Discovery

**Brian Wong, MD, PhD**  
VP Immunology and Discovery

**Kevin Baker, PhD**  
VP Pre-Clinical Development

**Harold Keer, MD, PhD**  
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**Amy Collins, PhD, JD**  
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**Lewis Williams, MD, PhD**  
Executive Chairman

Employees: 110  
Location: Mission Bay, San Francisco

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**THE LEADER IN BIOLOGICS INNOVATION**

FivePrime has engineered a unique suite of technologies to comprehensively mine the entire extracellular human proteome- the complete collection of secreted proteins and receptors- to discover therapeutic protein drugs and antibody targets. We have used these pioneering technologies to develop a pipeline of new protein and antibody therapeutics.

**BIOLOGICS DISCOVERY PLATFORM**

FivePrime has built the industry's most comprehensive platform for interrogating the extracellular proteome. Our platform allows us to do both *in vitro* and *in vivo* biologics discovery at an entirely new scale and speed. Our technologies enable screening of the *entire* human extracellular proteome - the definitive set of proteins from which all future biotherapeutics will be derived - through medically-relevant assays to identify the best proteins for specific clinical indications.

- Foundational Technology. At the core of our platform is our screening library, based on the world's largest human cDNA collection. Our screening library, now containing over 4,400 unique proteins, has been built to contain essentially all secreted proteins and extra-cellular domains of receptors and many peptide hormones. A large percentage of our library is generated from commercially unavailable cDNA's and approximately 15% are novel proteins or splice variants that are not in the public domain. Our library also contains proteins that must be engineered to be reliably secreted, such as proteins secreted through non-classical mechanisms and type II membrane proteins.
- Cell Based Screening. Through proprietary expression technologies and automation, FivePrime is able to express over 2,000 proteins per week at a greater than 90% success rate. These proteins are then fed into high-content cell based screening assays that are designed to model the disease state, using primary cells and employing upwards of 30 readouts in a single well.
- In Vivo Expression. These technologies enable rapid screening of secreted proteins *in vivo* in essentially any animal model. These technologies also provide for rapid validation and follow-up of *in vitro* hits, as well as scouting of PK and toxicology parameters.

<u>Cell Based Screening</u>	<u>In Vivo Technologies</u>
<ul style="list-style-type: none"> <li>• Screening library contains over 4,400 secreted proteins, peptides and receptors</li> <li>• Proprietary expression system produces functional proteins</li> <li>• High throughput assays with complex and diverse readouts</li> <li>• Human primary cells modeling the disease state</li> </ul>	<ul style="list-style-type: none"> <li>• Molecular approach generates sustained, high levels of circulating protein</li> <li>• Can use essentially any model, including disease models</li> <li>• Rapid validation of <i>in vitro</i> hits and initial PK, toxicology</li> <li>• Screening proteins <i>in vivo</i></li> </ul>

FivePrime's screening database contains the performance of each protein in more than 140 different assays, providing us a wealth of information on the specificity and activity of ligands and receptors by cell type. These data, combined with our ability to rapidly match receptors with ligands, provides powerful insights into molecular pathways, helps prioritize targets and in some cases can lead directly to new product opportunities.

For downstream work, FivePrime has built a strong scientific team, with years of experience in protein and antibody engineering, formulation, production and purification.

**PARTNERING**

FivePrime has collaborations with Johnson & Johnson's Centocor division in osteoarthritis and pulmonary fibrosis and with Pfizer in specific areas of oncology and diabetes. We seek additional discovery and development collaborations that will enable us to more fully exploit our robust biologics discovery platform and accelerate advancement of our pipeline.

## ONCOLOGY

### PIPELINE

**FP1039.** A Phase 1 study in advanced solid tumor cancers is underway to test the safety and tolerability of FP-1039. FP-1039 is a soluble fusion protein consisting of a portion of FGFR1 that is designed to neutralize the activity of multiple FGFs and FGFRs. Tumors of the breast, prostate, lung, ovary, colon and pancreas have been reported to have a strong dependence upon the FGF pathway for survival and growth. Clinically, activation of this pathway has been correlated with: 1) decreased survival and time to metastasis in several major cancers; and 2) angiogenesis that is resistant to anti-VEGF therapy. In pre-clinical studies, FP-1039:

- Has direct anti-tumor activity in a variety of *in vitro* and *in vivo* models, including patient derived xenograft models;
- Strongly inhibits both VEGF and FGF-induced angiogenesis *in vivo*; and
- Inhibits cancer stem cell proliferation.

**FPT040 and FPA005.** We are developing two additional compounds targeting growth factor pathways. FPT040 is a modified receptor that has high affinity towards a ligand that is known to be over-expressed in colorectal cancer. We are also developing an antibody, FPA005, that has been demonstrated to block activation of an important growth factor pathway *in vitro*.

**FPT069.** Currently in pre-clinical development, FPT069 blocks a pathway activated by IL-34, a novel cytokine discovered at FivePrime. There is evidence that inhibition of this pathway slows tumor progression in animals, inhibits angiogenesis and reduces bone loss from bone lesions in cancer. FPT069 is also being evaluated for use in autoimmune diseases.

### ADVANCED DISCOVERY

FivePrime is using the most medically relevant cancer cells and *in vivo* models to advance our oncology discovery programs.

- **Cancer stem cell screens** to identify proteins that increase the sensitivity of cancer stem cells to existing oncology therapies, drive cancer stem cells to differentiate into non-tumorigenic progeny and inhibit cancer stem cell proliferation and survival.
- **Primary cancer cells** to identify proteins that modulate known oncogenic pathways and stimulate cancer cell proliferation, survival, tumorigenicity and angiogenesis.
- **In vivo ligand traps** to directly assay for anti-cancer activity within the context of a living animal model. This approach is ideally suited to discover receptor ECD's that can inhibit the complex interactions between the tumor and host required for processes such as angiogenesis, immune escape and metastasis.

## PIPELINE AND THERAPEUTIC PROGRAMS

		Discovery	Lead Optimization/ Candidate Selection	Preclinical Development	Clinical Phase I
<b>Oncology</b>	FP-1039				
	FPT091				
	Pfizer				
<b>Immunology</b>	FPT069				
	IL-34				
	FPA008				
<b>Diabetes</b>	FPT097				
<b>OA</b>	Centocor				
<b>IPF</b>	Centocor				

### Metabolic Disease

FivePrime has active research programs in diabetes and obesity, including:

- **Glucose regulation** for factors that increase peripheral glucose uptake into muscle, liver and adipocytes. Initial efforts in this area have identified FPT038, a secreted protein that stimulates glucose uptake into muscle cells independent of insulin.
- **In vivo screening** in animal models of insulin resistance, obesity, lipid dysregulation and/or type 2 diabetes.
- **Adipocyte regulation** for proteins that modulate the energy expenditure and metabolic pathways of adipocytes and the differentiation of adipocyte precursor cells.

### Regenerative Medicine

Repairing and re-growing tissues has great medical promise and is uniquely suited to protein-based therapeutics given their prominent role in developmental biology. Areas where we have high on-going interest include:

- **Stem cells** for factors that promote stem cell survival and differentiation.
- **Cardiovascular** for proteins that increase cardiomyocyte survival and/or cardiac stem cell proliferation for treatment of acute myocardial infarction and congestive heart failure. Two proteins have been discovered thus far; both are therapeutically active in a myocardial infarct model.
- **Islet regeneration** for proteins that stimulate the survival and/or proliferation of pancreatic beta cells.
- **Intestinal bowel disease** for proteins that promote the survival and regeneration of intestinal epithelial cells. Two proteins have been discovered thus far; both are therapeutically active in an IBD model.

### Immunology

Our discovery efforts in immunology have been validated by our discovery of a new cytokine, IL-34 and the identification of its receptor. Current lead optimization work in this therapeutic area is focused on:

- **Tumor-associated macrophages** to discover proteins that stimulate the immune system to mount a cytotoxic response to cancer cells.
- **Modulation of T-regulatory cells** to regulate the immune response.
- **Anti-virals and anti-infectives** to increase the effectiveness of the innate immune response.