

**THE LEADER IN BIOLOGICS INNOVATION**

FivePrime is uniquely positioned to comprehensively mine the entire extracellular human proteome- the complete collection of secreted proteins and receptors- to find therapeutic protein drugs and antibody targets. We are using our pioneering technologies for protein drug discovery to build 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. The platform allows us to do both *in vitro* and *in vivo* biologics discovery at an entirely new scale and speed. We can rapidly screen 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, peptide hormones, and extra-cellular domains of receptors. 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 4,000 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 of certain factors and receptors by cell type as well as the regulators of biologic processes within specific cells. 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 Boehringer Ingelheim and Johnson & Johnson’s Centocor division in individual immunological diseases 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.

**MANAGEMENT TEAM**

**Lewis (Rusty) Williams, MD, PhD**  
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**Gail Maderis**  
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Executive Chairman

Employees: 88  
Location: Mission Bay, San Francisco

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**ONCOLOGY**

**PIPELINE**

**FP1039.** We expect to file an IND for our lead oncology compound, FP-1039, in Q2 2008. FP-1039 uses a novel mechanism to inhibit a pathway that is believed to be a key driver of cancer growth and maintenance. It is a modified receptor that can bind to multiple members within a growth factor family. Activation of this pathway has been correlated with: 1) decreased survival and increased risk of metastasis in several major cancers, 2) angiogenesis that is resistant to anti-VEGF therapy, and 3) cancer initiating cells maintaining their tumorigenicity. 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;
- Inhibits cancer stem cell proliferation;
- Reduces the number of metastasis in a lung metastasis model;
- Strongly inhibits both VEGF and FGF-induced angiogenesis *in vivo* and
- Increases the therapeutic effect of targeted therapeutics such as Avastin and Erbitux.

**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 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.

**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.

		Discovery	Lead Optimization/ Candidate Selection	Preclinical Development	IND Activities
<b>Oncology</b>	FP-1039				
	FPT040				
	FPT069				
	FPA005				
	FPT047				
<b>Diabetes</b>	FPT038				
<b>AMI/CHF</b>	FPT033				
	FPT057				
<b>IBD</b>	FPT042				
	FPT046				

**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:

- **ES cells** for factors that promote ES 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.
- **Macular degeneration, diabetic retinopathy and other eye diseases** for proteins that inhibit neo-angiogenesis, reduce inflammation or have neuroprotective activities.
- **Osteoarthritis.** Partnered with Centocor (J&J) in 2006.

**Immunology**

Our discovery efforts in immunology have been validated by our recent discovery of a new cytokine, IL-34 and the identification of its receptor. Current pre-lead 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.
- **Rheumatoid arthritis.** Partnered with Boehringer Ingelheim in 2006.
- **Pulmonary fibrosis.** Partnered with Centocor (J&J) in 2006.