Vivo Biosciences Project Meeting
Thursday, September 19th, 2013
Webinar

Cambridge Healthtech Associates
Ernie Bush (Scientific Director)
Dawn Van Dam (General Manager)
Amid Zand (Project Manager)

Abbvie
Eric Blomme (not on call)
John Burkhardt (not on call)

Amgen
Chuck Qualls (not on call)
Padma Narayanan (not on call)

Astellas
Jiro Seki (not on call)

Infinity
Alex Constan (not on call)
Nicole Hurst (not on call)

J&J
Monicah Otieno (not on call)
Peggy Guzzie-Peck (not on call)

Lundbeck
Jorrit Hornberg (not on call)

Pfizer
Yvonne Will
Gina Yanochko (not on call)
Andreas Maderna (not on call)
Lisa Marroguin
Andreas Giannakou
Ken Geles

UCB
Stephane Dhalluin (not on call)

Vivo Biosciences
Steven Schmid
Raj Singh

I) Welcome

The team members on the call introduced themselves.

Yvonne: Yvonne is a Steering Committee member from Pfizer. She has been involved with TEC for about 3 years and coordinates all Pfizer activities in the consortium. Yvonne is involved in early stage *in vitro* safety screening. She invited Ken, Andreas, and Lisa to the meeting from Pfizer.

Lisa: Lisa is involved in oncology-related mitochondrial biology studies in Yvonne's group and has been with Pfizer for 10 years. She is interested in 3D cultures and co-cultures.

Ken: Ken is the research project leader in the Bioconjugate Discovery and Development program at Pfizer. His team develops antibody drug conjugates. His group has early and late stage compounds in the pipeline and is looking for the best platforms to screen compounds for existing and new targets.

Andreas: Andreas has worked with Ken since 2010. His team's activities bridge the gap between *in vitro* and *in vivo* studies to develop more predictable end results. Andreas has worked for 3 years at Pfizer and for 4 years in academia focusing on 3D cell culture development.

Raj: Raj is the president and CEO of Vivo Biosciences and a cancer researcher. For more than twenty-five years he has focused on developing 3D cancer models. His new platform can be used in High Throughput Screening (HTS) of preclinical candidates using micro-tumor models.

Steve: Steve is the COO of Vivo Biosciences. He recently joined Vivo Biosciences to help with the commercialization of the technology. Steve's background is in cancer pharmacology and drug development. Steve has spent 6 years at Genzyme and 5 years at ILEX Oncology. He finished his postdoctoral fellowship at the University of Wisconsin School of Medicine.

II) Vivo Biosciences Presentation

Raj shared his desktop to present the slides. He gave an overview of his HTS micro-tumor platform and showed possible preclinical and predictive applications for a drug discovery and development program.

Raj shared the company background. The company's R&D efforts are supported by SPIR grants from NIH and NASA ($5M). The company has been offering products and services since 2009.

Raj shared a list outlining the company management team and board members.

Raj started the scientific discussions and argued for a need for better predictive models between cell-based HTS Discovery and Preclinical stages of pharmaceutical R&D.

To address those issues, many studies have been done to create more predictable 3D models. Raj compared Colony Assays, Cell Spheroids, and 3D Gel Layer models and discussed their limitations and problems.

To overcome these limitations, Vivo Biosciences has developed a 3D human derived culture system to replicate human tumor biology. Raj argued that the model, known as **HuBiogel,** creates fully human tumor models, supports multi-cellular growth and function, and exhibits a true tumor microenvironment.

Raj explained that the model is not synthetic and is derived from de-cellular human amnions. In the 3D HuBiogel, the cell culture is not denatured and is growth factor free. Raj also explained the unique properties and advantages of HuBiogel as compared to Matrigel and EHS Gels.

Using HuBiogel as a scaffold, Vivo Biosciences has created a fully robust 3D Micro Tumor Assay Platform. Commercial cell lines are mixed with the 3D HuBiogel to create micro tumors using automated production and culture protocols (1-3 days).

Ken: Is there any serum in the bioreactor? Have you tried any primary cell lines that have never been in serum?

Raj: Yes, we can use serum free culture media and primary cell lines. To keep the cells alive after forming the Micro Tumor beads, we put them in a media. When Vivo Biosciences does a construct, clients define the cell lines and media. Vivo Biosciences will never switch the media.

Raj shared different NCI-60 Micro Tumor Assay Models and various cell types. He discussed how they have successfully replicated slow and fast 3D growth, hypoxia, and host-tumor models. Raj mentioned that the media is changed every 3 days.

He further explained that viable tumors are delivered in 96/384-well plates and they can undergo multiple analyses. Possible analyses included measures of tumor growth, drug uptake, and tumor sensitivity as well as cell cycle parameters, RNA/DNA arrays, IHC, and biomarker analysis.

Raj compared examples of NCI tumor growth profiling using HuBiogel and Matrigel (with regular growth factor) and concluded that HuBiogel can distinguish slow vs. fast tumor growth better than Matrigel. It was also shown how different matrices induce different gene profiles in cells.

Raj mentioned that Vivo Biosciences has done about 20 case studies to show that HuBiogel is an effective *in vitro* assay and shared the case study results.

The case studies included:

- Standard Anti-Tumor Drug Screening
- NCI-30 Drug Screening Project with OSI
- 3D Tumor-Stroma Progression Model
- Micro Tumor Validation Collaboration with Novartis
- RTK Activation Pathway in 3D vs. 2D
- Phospho-Array Signaling Differences
- Microtumors are similar to xenotumors
- Gene Induction in MicroTumors
- Determining clinical relevance *in vitro* for PDx micro tumors with Champions Oncology
- Patient-Derived GBM Models

In conclusion, Raj highlighted that 3D MicroTumors provide *in vivo*-like results and proposed a technical plan and a business plan to the Steering Committee.

The technical plan included:

1. Evaluating select drug candidates
2. Screening a large compound library
3. Potential integration with HT genomic and proteomic program

The business plan included:

1. Validating new preclinical 3D tumor biology platform
2. Recognizing joint R&D interest and business opportunity
3. Expanding technology to multi-tissue toxicity applications

Similar to tumor technology, Raj added that HuBiogel can be used to grow multi-tissue toxicity models such as micro liver, 3D-Islets, and 3D skin. That technology was said to be in development at Vivo Biosciences.

III) Discussion and Q&A

Ken: Pfizer has proprietary PDx Models. Would we send you these models or can we have this technology in-house?

Raj: The most efficient way is to provide us with the PDx models; Vivo Biosciences will grow micro tumors and supply them in micro plates to Pfizer overnight. The tumors survive up to 4 weeks.

Ernie: Because of the proprietary nature of the cell lines, projects will be run on a one-on-one basis. CHA prefers the collaborative model but in this case, members prefer to move forward individually with their own cell system.

Ken: Have you grown lymphoma tumors as they are very difficult to culture *in vitro*?

Raj: Not yet.

IV) Action Items

1) Pfizer will discuss the technology internally and will propose a project.
