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I. Introduction

Good morning Chairman Latta, Ranking member Schakowsky, and members of the Subcommittee. Thank you for inviting me today to discuss Organovo and the capabilities of our 3D bioprinted human tissue models. Bioprinted 3D human tissue models are disrupting the drug discovery process because they give researchers and regulators new tools and capabilities to make drug discovery safer, speedier, more likely to find breakthrough drugs in new areas, and less costly. Bioprinting also enables future implantable therapies to restore or cure failing organ function and address the long waiting lists for organ transplant.

II. What is 3D Bioprinting?

An office printer uses ink to print on paper, and industrial 3D printers use liquid plastic or metals to print machine parts or prototypes. We use human cells to make "bio ink" that is deposited by a "bio printer" which layers the bio ink onto a surface to form organic, living 3D human tissue. Bioprinted research model tissues have been shown to replicate the key elements, architecture, and function of living native human tissues. Bioprinted tissues for transplant have been demonstrated to have powerful potential to treat serious illness by direct transplant into patients. I have submitted slides along with the written testimony that will help you visualize the manufacturing process, where we fit into the current drug discovery process, the current progress in transplantable tissues, and examples of the peer reviewed data we have used to validate the capabilities of our bioprinted tissues.

III. What are 3D Human Tissue Model Capabilities to Speed Safer Drugs to Patients?

Our 3D human tissue models are currently disrupting drug innovation in three essential ways:

1) providing commercially available 3D human liver and kidney models that effectively bridge the gap between preclinical (animal) testing and clinical (human) trials to improve the predictability, safety, and speed of the discovery process while also lowering the cost of bringing new therapies to patients;

2) modeling known diseases, often for disease without good models today where patients lack available therapies, to help researchers best target potential medicines; and

3) platform technology needed to develop first in class implantable regenerative medicine therapies that will one day meaningfully restore or cure failing organ function.

IV. Company Background

Founded in 2007, we are in San Diego, CA and have grown from 7 to nearly 120 employees in 10 years. We perform research, build 3D bioprinters, print tissue models, and run our testing services out of our 45,000 sq. ft. headquarters building. Our customers and partners include almost half of the world's top pharmaceutical companies. To date we have overcome the challenges of starting, funding, commercializing and growing a small business to develop 3D bioprinted platform technology with multiple potential applications. There is a diversity of organ tissues to replicate (liver, kidney, cancer tumor models, lung, skin, etc..) and potential commercial applications beyond drug discovery – such as cosmetics and chemical testing. There are wide ranging applications for the Department of Defense including everything

from delivering testing tissues for developing protections against biological attack to creation of tissues to replace function lost by wounded warriors.

Recognizing the broad potential, we have partnered with a number of top academic centers across the country who now use our bioprinters on site – including one at the National Institutes of Health (NIH). Our primary business is not selling printers, but we work closely with qualified partners so that they can perform specialized research projects – such as bioprinted breast cancer tumor models built at Oregon Health Sciences University or cardiovascular tissues at Yale University School of Medicine.

V. Disrupting the Drug Discovery Process for Researchers and Regulators

From 1990 to 2010, 73% of phase 3 clinical trials failed due to toxicity or lack of efficacy. In 2012 alone, 10 late stage clinical trial failures cost innovators $7-10 Billion in losses.[i] In addition to drug companies seeking to make the discovery process more efficient and predictive, the Food and Drug Administration (FDA) also has recognized the need for improved drug discovery tools. A 2011 report by FDA, entitled ''Advancing Regulatory Science at FDA'', prioritized toxicology testing and the development of models of human adverse response as one of the areas of regulatory science where new or enhanced engagement by the agency is essential to the continued success of the public health and regulatory mission[ii].

While the regulatory landscape has remained static, Organovo's 3D human tissue models are currently being used by innovators as a high content screening tool to improve so called "lead candidate selection" – essentially help prioritize which therapies should progress from the lab to human clinical trials. A high content screening effectively allows researchers the benefit of an organ biopsy in a dish without having to take one from an actual patient. Our tissue models give researchers the ability to look to see if the drug is working, how it is being metabolized over time, and whether it is producing toxic side effects. These models also are being used to help improve the safety and efficacy of potential drugs currently progressing through human trial phases.

Over the last few years, we have developed a breadth of peer reviewed data on our own and in collaboration with our research partners. We have been able to show that 3D human tissue models:

- Closely mimic human tissue composition and physiology -- including biochemical and histologic outcomes;
- Retain key aspects of native human liver for at least six weeks;
- Capture complex multi-cellular events that are not typically captured by traditional 2D in vitro systems; and
- Can detect the liver toxicity of about 70% of the compounds that have historically not been predicted to be liver toxic and thereafter had a surprising failure during development or withdrawal post-marketing.

Just this week, we released even more data about our liver and kidney tissue models capabilities at the Society of Toxicology Conference in Baltimore[iii].

We also believe 3D human tissue models can be used to help improve the post market safety understanding of approved products. The attached slides give validating examples where our 3D human tissue models are proven to show toxicity signals for drugs approved and later identified by the FDA as well as no toxicity signals in approved drugs that are proven to show no toxicity signs in humans.

For example, a July 2016 peer reviewed study using 3D bioprinted liver tissues modeled drug-induced liver injury (DILI) to investigate the effects of Trovafloxin – a drug withdrawn from the market due to acute liver failure in patients.[iv]

- This study by researchers from Organovo and Roche found that 3D bioprinted liver tissues identified significant Trovafloxin liver toxicity after just seven days of exposure.

- In contrast, Trovafloxin does not show strong toxicity signals in common traditional 2D in vitro systems. The study provided new evidence that 3D bioprinted tissues can better model the effects of chronic drug dosing or conditions that develop over extended periods of time.

In addition to bioprinted liver tissues, we recently introduced a kidney model for our customers that can model renal toxicity. Detecting kidney toxicity previously has been very difficult to model in vitro. Most researchers still rely on non-human animal models. Our tissue level construction and architecture allows for study of complex drug-induced phenotypes involving multiple cell types. We can provide a number of toxicity readouts including clinically relevant renal injury biomarkers.

Just last year, National Institutes of Health (NIH) Director Francis Collins predicted before the Senate Appropriations Committee that 3D bioengineered tissue will soon speed drug discovery, improve its safety, lower its cost, and largely replace the need for animal testing. Furthermore, a December paper co-authored by the head of FDA's Center for Toxicological Research (NCTR), an Associate Vice President of Toxicology at Merck, and an esteemed researcher in liver biology from Life Net Health not only showcased our technology's capabilities but also its relevance to modernizing the drug discovery process[v]. It identified 3D human tissue models represent the future for "candidate selection" where companies must prioritize drug candidates and resources needed to progress from pre-clinical to phase 1 human trials.

The authors validate the innovative role Organovo's 3D human tissue model capabilities can add to the drug discovery process*: "Bioprinting technology that recently has been developed represents a significant innovation in the study of drug-induced liver injury (DILI), as it addresses many of the shortcomings associated with traditional in vitro culture models and animal models."* They also state that 3D bioprinted tissues *"exhibit a broad range of highly differentiated in vivo like features and functions."*

The authors reference results from Organovo's drug-induced liver injury studies that have shown *"very good reproducibility and concordance with observed outcomes in vivo at the functional and histological levels" and that treatment of the bioprinted human liver model with known fibrotic agents "mimicked closely that of patient liver samples with drug-induced fibrosis."*

The authors conclude that both researchers and regulators should be adopting the use of the 3D bioprinted human tissue models: "*The insertion of such high performing, accurately predictive, well-qualified assays for DILI prediction at the right stage and in the appropriate context can favorably impact drug development to enhance success, shorten timelines, reduce the needless use of animals, provide more value from each animal study (and human trial) that is conducted, and help to reduce overall costs by spotting and weeding out compounds with liabilities earlier. It is imperative that we step up quickly to the challenge of prioritizing the most promising tools, evaluating performance critically and collaboratively,*

and qualifying and integrating these tools wisely to improve success and reduce needless waste of animals."

We are pleased that both the 21st Century Cures legislation and the draft Prescription Drug User Fee Act (PDUFA) VI agreement take steps to encourage the use and adoption of new drug discovery tools. However, they can be fine-tuned to accelerate the adoption of currently available technologies, with existing validating proof, that can be impactful by driving wider adoption as quickly as possible versus longer term technologies that will not be ready for use until PDUFA VII or later. In addition to being "ready to go', FDA should also prioritize adoption of models that are proven to detect toxicity not identified in non-human animal models or detect or predict toxicity of known clinical failures.

We are grateful that Committee members led by Congressman Chris Collins (R-NY) introduced legislation last year -- the Patient Safety and Toxicology Modernization Act, requiring FDA to issue guidance by the end of 2018 regarding the development and use of novel tools for toxicology and efficacy testing including, but not limited to, three-dimensional human tissue models. The guidance should address the use of such models for preclinical, clinical, and post-market safety and efficacy testing, labeling, or other uses by product sponsors and the Food and Drug Administration. We hope that the Energy and Commerce Committee includes this legislation in PDUFA VI to ensure FDA prioritizes adoption of commercially available and proven discovery tools that can speed and lower the cost of drug discovery.

VI. Regenerative Medicine Therapies to Restore Organ Function

Organovo's 3D bioprinting technology also can be used to develop first in class implantable tissue therapies that cure or meaningfully restore a patient's organ function. Advancement of such therapies will help close the gap between patients who are waiting for organ transplants and those who actually receive them. In 2015 there roughly were 120,000 Americans waiting for an organ transplant and just 30,000 transplants performed[vi]. These statistics do not include those not allowed on the list in the first place.

Organovo recently presented data showing survival and sustained functionality of our 3D bioprinted human liver tissue when implanted into animal models[vii]. The preclinical data showed:

- rapid vascularization and tissue engraftment, and evidence of function and durability of our 3D bioprinted human liver tissue over several weeks;

- evidence of stable production of key human liver proteins in the animal bloodstream, and tissue staining for key human metabolic enzymes; and

- the capability of this tissue to potentially treat inborn errors of metabolism.

The FDA will soon have cell-based bioprinted tissue therapy applications under review. We are grateful that the 21st Century Cures legislation not only created a new regenerative medicine pathway at FDA without lowering safety standards, but also provided greater clarity on how FDA will review so called combination products. One way to enable bioprinted tissues to impact the greatest number of patients in the fastest prudent time frame is to continue to pursue regulatory clarity for regenerative medicine products, in particular tissue-based biological products currently regulated by CBER. Global regulatory agencies in Europe and Japan already have implemented regenerative medicine regulatory pathways.

Clear, timely, and collaborative implementation of relevant 21st Century Cures provisions will help ensure that regenerative medicine innovation, research, and clinical trials remain in the U.S.

We look forward to working with the Committee and FDA to ensure that these life-saving provisions are implemented thoughtfully to make sure companies like Organovo understand what data is needed to successfully speed these first in class therapies safely to patients.

Thank you again for inviting me to participate in today's hearing. I am happy to answer questions related to my submitted testimony or slides.

About Organovo

At Organovo, we design and create functional human tissues using our proprietary three-dimensional bioprinting technology. Our goal is to build living human tissues that are proven to function like native tissues. With reproducible 3D tissues that accurately represent human biology, we are enabling ground-breaking therapies by:

- Partnering with biopharmaceutical companies and academic medical centers to design, build, and validate more predictive in vitro tissues for disease modeling and toxicology.

- Giving researchers and regulators something they have never had before – the opportunity to test drugs on functional human tissues before ever administering the drug to a living person; bridging the gulf between preclinical (animal) testing and clinical (human) trials.

- Creating functional, three-dimensional tissues regenerative medicine therapies that can be implanted or delivered into the human body to repair organ function or replace damaged or diseased tissues.

About Keith Murphy

Keith Murphy, Chairman and Chief Executive Officer

Keith Murphy co-founded Organovo in 2007 and has led all company operations since that time. He co-invented the company's NovoGen MMX bioprinter platform and grew the company through early investments and corporate partnerships. Since going public in 2012, the company has focused on the development of three-dimensional liver, kidney, and cancer tissues. The most advanced program, liver tissue, has grown to encompass a range of applications from commercial use for pharmaceutical toxicology prediction to the preclinical development of human 3D liver patches for transplant patients. Prior to co-founding Organovo, Mr. Murphy spent 15 years in biotech, including ten years at Amgen in roles of increasing responsibility, with four years as the Global Operations Leader of denosumab, now marketed as Prolia & Xgeva ($3B+ annual sales). He holds a B.S. in chemical engineering from the Massachusetts Institute of Technology and is an alumnus of the UCLA Anderson School of Management. He currently serves on the Boards of the Torrance Memorial Medical Center Foundation and the California Life Sciences Association.

[i] FDA.gov; Pharmaceutical Research Manufacturers of America, Profile 2011; EvaluatePharma; Parexel Sourcebook 2012; CDER Report to Nation; Tufts Center for Drug Discovery

[ii]Advancing Regulatory Science at FDA
https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RegulatoryScience/UCM268225.pdf
[iii]Organovo and Its Customers Present Data Supporting 3D Bioprinted Liver and Kidney Tissues for Drug Toxicity Testing http://ir.organovo.com/phoenix.zhtml?c=254194&p=irol-newsArticle&ID=2253403
[iv] Bioprinted 3D Primary Liver Tissues Allow Assessment of Organ-Level Response to Clinical Drug Induced Toxicity In Vitro http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0158674
[v] The Promise of New Technologies to Reduce, Refine, or Replace Animal Use while Reducing Risks of Drug Induced Liver Injury in Pharmaceutical Development https://academic.oup.com/ilarjournal/article-abstract/57/2/186/2806701/The-Promise-of-New-Technologies-to-Reduce-Refine
[vi] Organ Donation Statistics https://www.organdonor.gov/statistics-stories/statistics.html
[vii] Organovo Presents First Preclinical Data on 3D Bioprinted Human Liver Tissues at TERMIS-Americas Meeting http://ir.organovo.com/phoenix.zhtml?c=254194&p=irol-newsArticle&ID=2229241