April 14, 2011
Nanotechnology: Oversight of the National Nanotechnology Initiative and Priorities for the Future

Key Points of Testimony

Commercialization of Nanotechnology

- The investment in nanotechnology by the NNI and private industry has confirmed that nano-enabled products are a means to solving some of humanity's most vexing challenges and a critical driver of future economic growth.
- To translate this investment into viable products and new industries, manufacturing R&D must go hand-in-hand with scientific discovery to ensure that U.S. manufacturers can quickly transform innovations into processes and products.
- Due to the historic emphasis on funding and commercialization of inorganic nanomaterials, there is an even larger gap to commercialization for nanotechnology in life science applications.
- Nanomedicine technologies have tremendous potential for *transformational results* – disruptive changes over and above current methods and strategies for healthcare, with wide-ranging implications on how we detect, prevent and treat disease. To maintain the dominant position of the U.S. in healthcare innovation and quality of life, we must close the gap from proof-of-concept to commercial viability for nanomedicine platforms.
- Nanotechnologies must be brought to market responsibly; meaningful nanoparticle standards to assess physio-chemical properties of nanomaterials for environmental and health implications are necessary for sustainable product development.

Recommendations

- Increase the support of nanomanufacturing initiatives. We are in strong agreement with the PCAST recommendation to increase the focus on nanomanufacturing to accelerate technology transfer to the marketplace.
- Ensure that nanomedicine platforms are included within the Signature Initiatives of the NNI.
- Support the development of reference materials, test methods, and other standards that provide broad support for industry production of safe nanotechnology-based products. We strongly support the establishment of a "particle foundry" to meet these needs.
- Strengthen the NNCO to ensure the breadth of investments and advancements in nanotechnology R&D are translated into viable commercial products.

Liquidia's PRINT® nanotechnology platform

- The proprietary PRINT nanofabrication technology was pioneered at the University of North Carolina and is being commercialized by Liquidia Technologies, a small venture-backed company in Research Triangle Park, North Carolina.
- The PRINT technology offers unprecedented control of particle size, shape and chemistry in a highly consistent and scalable roll-to-roll manufacturing process.
- Liquidia is currently focused on commercializing applications in vaccines, inhaled therapeutics and oncology. The company's first product was successfully introduced into Phase 1 clinical trials in Q4 2010.

Written Statement

Seth Rudnick, M.D., Chairman of the Board
Joseph DeSimone, Ph.D., Founder

We are in strong agreement with the general recommendations by PCAST focused on Program Management, Outcomes and EH&S. In particular, strong leadership through the National Nanotechnology Coordination Office (NNCO) is needed now more than ever to coordinate the broad investments and outcomes and to ensure the investments in nanotechnology innovation can be successfully transformed into commercial products. Liquidia's current efforts towards commercial implementation of our nanotechnology platform is the direct result of the strong support that the NNI has received to date.

Let us summarize what we have been able to accomplish as a direct result of our previous support from various agencies through the NNI as well as provide some thoughts and refinements regarding specific aspects of the PCAST recommendations.

Introduction to Liquidia's PRINT Nanotechnology Platform

Many innovations have emerged from the NNI to date, especially at the interfaces between disciplines. Indeed our particular nanofabrication innovation has been to co-opt the lithographic manufacturing technologies from the microelectronics industry and apply them to making new vaccines and medicines. This work was pioneered in the Department of Chemistry at the University of North Carolina at Chapel Hill (UNC) and Liquidia Technologies, Inc., a start-up company spun out of UNC (www.liquidia.com). The technology trademarked as PRINT (Particle Replication in Non-wetting Templates) marries the slow, yet highly precise batch based process used to make integrated circuits with the volume production of the film and printing industry. This creates a proprietary, US-based roll-to-roll manufacturing process useful for making vaccines and therapeutics that are in nanoparticle form. The PRINT manufacturing platform offers unprecedented control of particle size, shape and chemistry in a highly consistent and scalable roll-to-roll manufacturing process. The UNC team is funded by NIH, NCI, NSF, DOE, DARPA and ONR and the Liquidia Team has been largely venture financed (Canaan, NEA, and others) with a few significant grants awarded from NIST ATP and TIP programs. Just recently, Liquidia received the first ever equity investment by the Bill and Melinda Gates Foundation in a for-profit biotech company. Liquidia has a focus in vaccines (influenza, malaria, cancer, etc), respiratory diseases (COPD, PHT, CF, Asthma) and oncology, and successfully introduced its first product into Phase 1 clinical trials in Q4 2010. As such, we believe PRINT is the first nanotechnology *platform* that is now cGMP compliant.

Specifically for nanomedicine, the ability to manipulate size, shape, chemistry and modulus of nanomaterials can have wide-ranging impact on how we diagnose and treat disease. New abilities to tune these features can provide researchers with a more thorough understanding of "how" and "why" cellular and organ systems react, allowing scientists to build highly efficient tools that can safely operate inside the body. New technologies that have the power to control size, shape, and other functionalities are currently being developed and have shown remarkable promise, but significant investment in *scaling-up* and producing engineered nano-structures in a *cGMP* environment is necessary to bring innovations to commercial reality. What the latest advances in the field brings is the precision necessary to improve safety and to engineer new products with enhanced capabilities. This is exactly what the regulatory agencies have asked for: Increased reproducibility and precision, which is readily accomplished via Liquidia's PRINT technology.

Recommendations and Refinements to the PCAST Report
With this perspective and background, we have the following comments that we would like to make:

Unmet needs to advance the field of nanoscience and technology

- Nanotechnologies must be brought to market responsibly; meaningful nanoparticle standards to assess physio-chemical properties of nanomaterials for environmental and health implications are necessary for sustainable product development.
- There is a need for "qualified" nano- and micro-materials with control in particle size, shape and chemical composition and that are available at a scale useful for a broad range of scientific studies. The need for such "qualified" materials is different than the need being fulfilled by the nano-standards being developed by NIST which are mainly useful for very high-end technology needs, like the calibration of measurement instrumentation. Rather, "qualified" materials are materials that are almost of the same quality as the standards being developed by NIST but meet additional specifications to allow for utility across differentiated industries, including larger quantities at lower costs than that associated with NIST calibration standards.
- Additionally, a set of well characterized materials (environmental and health studies) that accurately represent the types of nanomaterials that are incorporated into products is needed to address many of the concerns voiced by the public. While EH&S research has always been a focal point for the NNI, we need to ensure that the nanomaterials used for this research are the same classes of materials used for consumer products and are tested in a relevant context.
- Liquidia's PRINT technology is one example of a breakthrough in particle manufacturing (40 nm in size and greater) that allows complete control in particle size, shape and chemical composition. The PRINT technology is particularly useful for generating a host of organic nanomaterials, a unique capability that is crucial for evaluating life science applications. Because of the roll-to-roll nature of the PRINT manufacturing process, one can allow researchers to have access to materials in meaningful volumes useful for many real world studies that NIST calibration standards are not suitable for. For example, important studies are needed and could be accomplished if "qualified nano-standards" were available such as aerosol standards (for inhalation studies, particulate distribution studies in cities and buildings, etc); environmental standards (for ground water fate studies, etc) and organic materials for *in vivo* biodistribution studies.
- It is recommended that the NNCO consider the establishment of a **Nanoparticle Foundry** much in the way that the Department of Energy through Lawrence Berkeley National Laboratory established the Molecular Foundry. The establishment of the **Nanoparticle Foundry** would address a key bottle neck for the generation of ideas and would play an important role in establishing our Nation's preeminence in nanomanufacturing which is crucial to establishing and growing jobs in the US.

Unmet needs for commercialization of nanoscience and technology

- Nanomanufacturing is the means through which the Nation will realize the benefits of nanotechnology. A major opportunity exists to leverage the past ten years of NNI research platforms and establish programs to translate this knowledge into viable products through the advancement of nanotechnologies. Nanomanufacturing R&D must go hand-in-hand with scientific discovery to ensure that U.S. manufacturers can quickly transform innovations into processes and products and that the investments made to date can be realized in the form of revenue and job creation
- Currently, private investment in nanotechnology is hesitant, weighing the risks of this relatively new field where considerable investment has already taken place in academia, which has yet to fully validate and deliver cost-effective and commercially viable platforms. Government funding in Nanomanufacturing is needed to realize the investments that have already been made. Bridging the gap from proof-of-concept to

commercial viability will provide the risk mitigation needed to encourage the private sector to support and further develop nanomedicine platforms.

- Nanomanufacturing developments need to strongly focus on manufacturing issues unique for the applications in the life sciences. Based on the current recommendations and NNI strategic plan, the nano manufacturing foci are largely devoid of materials and processes destined for use in life sciences.
- Targeted, government-driven funding can make a crucial difference in the scale, breadth, and time horizon of industry-driven R&D for nanomanufacturing. In the US, the largest funding opportunities that seed commercialization activity are the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. These programs are extremely limited in the terms of time and budget needed to support innovation in technology infrastructure. Transitioning a prototype process to a viable commercial scale is an effort that requires capital expenditure and timelines well beyond that of the SBIR and STTR programs, which in most cases offer a $100K phase I effort for a 6-month to 1 year effort. In addition, many nanotechnology based businesses are venture backed, requiring significant capital for pre-clinical or proof-of-concept studies prior to revenue. These companies are often not eligible for SBIR and STTR programs due to ownership requirements.
- The regulatory pathways for nanomaterials should be made explicit; the pathways should be scientifically based and it should be made clear which of the current regulatory pathways are already adequate for commercial approval. The issue is particularly applicable to therapeutics by the FDA but are inclusive of other agencies as tools become available
- One of the more important non-nano specific issues that need to be addressed to facilitate the development of such industries of the future is the US Patent Office. The USPTO is bogged down, with timelines to patent issuance being longer than ever in history. Such delays cause uncertainties and uncertainties inhibit private and corporate investments in new companies. This inefficiency is in stark contrast to recent announcements in China and other foreign competitors who are massively increasing the funding of their patent offices for rapid turnaround and issuance.

In conclusion, nanotechnology has the undeniable potential to create entirely new industries and products that will positively impact our environment as well improve the quality of life and prevent disease. But we cannot just innovate, we need to scale our inventions to realize this potential, creating jobs and economic prosperity. Perhaps no one has stated this more clearly than Andy Grove recently in an op-ed in Bloomberg News:

> Startups are a wonderful thing, but they cannot by themselves increase tech employment. Equally important is what comes after that mythical moment of creation in the garage, as technology goes from prototype to mass production. This is the phase where companies scale up. They work out design details, figure out how to make things affordably, build factories, and hire people by the thousands. Scaling is hard work but necessary to make innovation matter.
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> Andy Grove, July 1, 2010

Thank you for considering our comments.
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