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The Life Sciences Executive Network at The Sarian Group Presents

BIOTECH BULLETIN | SUMMER 2016

Tracking The Pulse of the Philadelphia Life Sciences Industry

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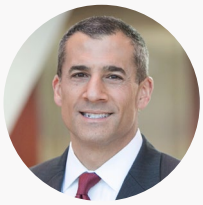
FOUNDER



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Stay up to date on the pulse of the Philadelphia Life Sciences industry with our *Biotech Bulletin*. This is a quarterly newsletter, with data and perspectives from local leaders within the industry. Greg Sarian of The Sarian Group is the author of the Biotech Bulletin. Each issue will include insight on the latest industry trends, performance metrics on local biotech companies as well as current acquisitions and IPO news in this area.

TOMORROW'S CURES COME FROM TODAY'S INVESTMENT

by Jennifer Riley | Managing Director, BRAVOGROUP

There's no question that the cures and treatments of tomorrow will come from the medical research innovations of today. But turning innovations into answers doesn't just take intelligent researchers and scientists armed with the latest technology. It takes quite a bit of investment.

It takes more than 10 years and more than $2.6 billion to research and develop a new medicine, according to the Tufts Center for the Study of Drug Development. However, there are misconceptions about where the funding comes from—even from policymakers.

Traditionally, funding comes from a mix of public and private sources, but the mixture has changed over time. For the last three decades, the public and lawmakers have consistently attributed all medical research singularly from the National Institutes of Health—a misconception that is fanning the flames of the drug pricing debate.

Granted, NIH is the largest biomedical research agency in the world and its work and funding have helped Americans (and the world) live longer and healthier lives. But as you know, public dollars only go so far. And while many nonprofit interest groups now disburse research grants, their reach is limited by the amount of donations they receive.

For example, in 2014, NIH awarded $23 billion for grants and contracts. Its $30 billion total budget largely has remained flat from 2003 to 2012, which, in real terms, resulted in a 22% decline in purchasing power, the agency has testified before Congress. That translates into funding fewer research proposals: In 1999, 34% of all research proposals to NIH were funded; in 2012, only 19% were, the agency reported.[1]

This is just one reason why the biotechnology industry has stepped in to ensure innovation and research continue to march toward developing new cures and treatments. To put it in context, the global biopharma industry spent $142 billion on research and development in 2014 or six times more than the NIH did, according to analysis done by the Biotechnology Innovation Organization. In a 2015 study published in the Journal of the American Medical Association, Johns Hopkins University researchers found that the number of clinical trials funded by companies increased 43% from 2006 to 2014 while the number of NIH-funded trials decreased 24% over the same period.

In contrast, over the last 15 years, biopharmaceutical companies committed more than $500 billion in R&D; in 2014 in the U.S., research investment totaled $51 billion, up from $15 billion in 1995. In the U.S. alone, the biopharmaceutical industry spends five times more on research and development than the aerospace industry and 2.5 times more than the software and computer industry.

We continue to make these life-saving investments in the face of long odds. And as an industry, we must continue to actively support increases in NIH funding, as well as educating our policymakers on the significant private investments that ultimately fuel tomorrow's cures.

References

1. NIH (2013). Research Portfolio Online Reporting Tools: Funding Facts. Search conducted on Mar. 11, 2013 seeking success rates across the entire NIH for all research grants.

2.Pharmaceutical Research and Manufacturers of America. "*2015 Profile Biopharmaceutical Research Industry.*" (2015): PDF.

ALTERNATIVES TO LIVE ANIMAL USE IN MEDICAL DEVICE RESEARCH

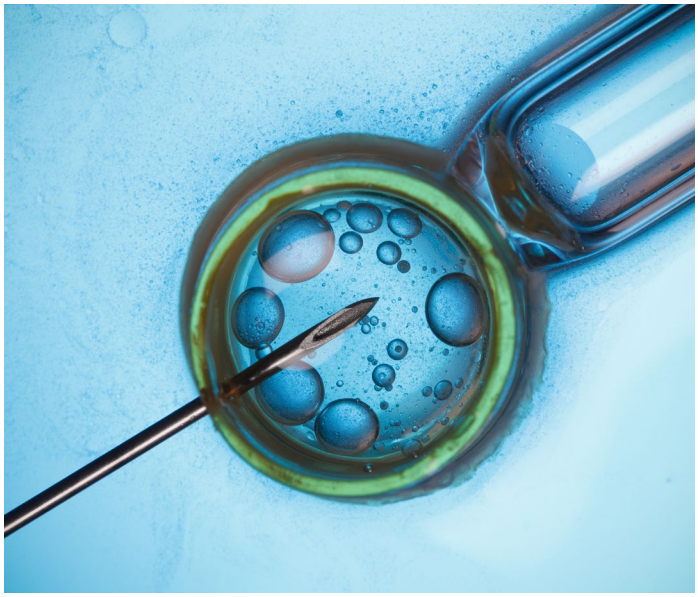
By Amelia Zellander, PhD | Founder, Scigofer, LLC

Animals are frequently used to demonstrate the safety of medical devices for human use. A sizable portion of the United States population, sometimes represented by groups like People for the Ethical Treatment of Animals (PETA) or New England Anti-Vivisection Society (NEAVS), objects to the use of animals in scientific research. Further, data from non-humans may not always predict safety outcomes in humans. Alternatives to animal testing exist, but as with *in vivo* testing, *in vitro* testing has its drawbacks. This article reviews recent dialogue in the scientific community concerning alternatives to animal testing.

In both the US and Europe, various organizations encourage researchers to replace, reduce, and refine animal experiments. This concept is referred to as the 3Rs. Among others, this idea has been addressed by the National Institute of Environmental Health Science, US Department of Agriculture, European Partnership for Alternative Approaches to Animal Testing (EPAA), and *In Vitro* Testing Industrial Platform (IVTIP). In 2013, IVTIP published a summary of their discussion on alternatives to animal testing. With *in vitro* assays, a wider range of samples could be tested with potentially lower cost and regulatory constraints as compared to animal studies. However, researchers may need to develop multiple *in vitro* tests to replace a given animal test. This could lead to an increased volume of data, and the risks and costs associated with that are unknown. Furthermore, validation times for new *in vitro* assays are unknown, and regulatory guidance may need to evolve to accommodate the new tests. To support implementation of animal test alternatives, the IVTIP group recommended:[1]

- Identifying best practices for faster development, stakeholder acceptance, and implementation
- Organizing a database of past animal study data
- Standardization of *in vitro* assays

Toxicology studies for medical products often involve animal testing. However, a new bioinformatics tool could change the future of toxicology. The Human Toxome Project, funded by National Institutes of Health, is developing a bioinformatics tool for pathways of toxicity (PoT). PoT refers to the cellular processes that mediate adverse outcomes of toxicants. The desired project outcome is a consensus framework and community database that allows toxicologists to map the human toxome. The PoT database could potentially become a key reference for toxicology studies and possibly reduce animal use. Mainstream toxicology testing involves introducing an agent to an animal and later observing the outcome. Since expected toxicity related outcomes could vary with unknown agents, knowledge of PoTs may help to identify adverse outcomes for unknown agents. However, challenges with PoTs must be addressed. For example, most agents interact with multiple targets in a biological system.[2]



The US Food and Drug Administration outlines its recommendations for the biological evaluation of medical devices in April 2013 draft guidance titled "Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing". *In vitro* testing is recommended to evaluate cytotoxicity. The following potential tests may involve the use of live animals: sensitization, hemocompatibility, genotoxicity, carcinogenicity, reproductive and developmental toxicity, and biodegradation. A range of *in vitro* tests have be proposed to replace live animal use. For example, the monocyte activation test (MAT) was developed to replace the rabbit based pryogenicity test. MAT is based on the knowledge that certain pyrogens, fever inducing agents, induce the secretion of selected biological agents including certain interleukins and tumor necrosis factors. Blood is the test material. MIMIC is an *in vitro* test for immunogenicity. FDA may request immunogenicity testing for submicron medical device components. The system, consisting of human immune cells placed in engineered tissue constructs and mimics the human immune system. Data from selected vaccines and biologics correlated well the data obtained from MIMIC.[3] The following websites can assist researchers in identifying alternatives to animal use:

- alttox.org
- altweb.jhsph.edu
- gopubmed.org

Some medical device tests investigate safety during the practical use of the device. When engineered or cadaver models are not suitable, live animal models may be deemed appropriate. Theoretically, an appropriate engineered model could be developed when cadaver models do not suffice. However, researchers must be mindful of the cost associated with creating and validating an engineered model.

In the US, both the Animal Welfare Act and Public Health Service Policy require researchers to consider alternatives to animal use. An increase in validated and cost effective *in vitro* alternatives may inspire greater acceptance and use.

References

1. Ashton, R., et al., *State of the Art on Alternative Methods to Animal Testing from an Industrial Point of View: Ready for Regulation?* ALTEX 31(3): p. 357–363.
2. Bouhifd, M., et al., *The Human Toxome Project.* ALTEX 32(2): p. 112-124.
3. Burm, S., et al., *Alternative Methods for the Use of NonHuman Primates in Biomedical Research.* ALTEX 31(4): P. 520-529.

A SPOTLIGHT ON INFRASCAN, INC.

A CONVERSATION WITH DR. BARUCH BEN DOR, A LEADER IN THE MEDICAL DEVICE INDUSTRY

Greg Sarian recently had the pleasure of having a conversation with Dr. Baruch Ben Dor, CEO and Board Member of InfraScan, Inc. InfraScan, Inc. is a medical device company that invented and distributes hand-held diagnostic devices for head injury and stroke assessment based on Near-Infrared (NIR) technology. The InfraScanner enables clinicians to effectively, conveniently, and accurately detect intracranial bleeding in patients with head trauma. Dr. Ben Dor holds a Ph.D. in physics and is a graduate of the highly prestigious Talpiot program of the Israeli Air Force. His experience in the electro optics field dates to 1988, in both the defense sector and in the medical device industry.

GREG SARIAN: **When you think about InfraScan, what is your primary area of focus? What are your main goals for your company to achieve here in 2016?**

BARUCH BEN DOR: InfraScan is in the field of triage and helping in the resuscitation of head trauma in emergency medicine environment. So, InfraScan's first product is a hand held device that helps in detecting brain bleeds in field conditions. We started first with the U.S. military, but we're also working with emergency medicine services and of course internationally. Currently, we are in a two prong effort. One, is we've finished successful fielding of a couple of hundred systems with the U.S. Marine Corps. And now we're in working with other services of the U.S. Military, especially the U.S. Army and trying to get that adopted by other services. On the other side, we are focusing on developing our next generation product.

GREG SARIAN: **So, when you look forward Baruch, at the next 12 to 18 months, what are the greatest opportunities for InfraScan and what are the biggest hurdles you're trying to overcome?**

BARUCH BEN DOR: I think we have three main areas that we are focusing on. First is the U.S. Military and especially U.S. Army, which is at least five times bigger than the Marine Corps. So, we believe this is a great source of opportunity for us. Another focus is this product has phenomenal potential in international markets—and we have had good success in large countries such as Russia or India, but our biggest potential we believe will be in China. So we're now going through Chinese FDA processes—which we hope to finish later this year; and I hope that could hold great potential for us. And the last field that we believe that the product has—we have phenomenal opportunity is the field of sports medicine—the product was just adopted by the National Olympic Committee in Russia as part of standard of care for athletes and the Russian delegation to Rio Olympics is going to bring a couple of InfraScanners with them.

GREG SARIAN: **What are your greatest challenges? What are the hurdles that you have to overcome in the next year or so?**

BARUCH BEN DOR: Well, the biggest challenge that we have, and this is true for some companies that bring innovative products to the market, is that beyond selling the product, you're really selling a concept. So we have a lot of work to do on educating customers and not only selling to customers. It's always easier to sell a better mousetrap…something that customers are familiar with. When you are selling innovative concepts, it is much more challenging. As always the main issue that is pretty common to all Life Science Companies is the very substantial regulatory hurdles that, with time, are becoming only worse and worse. We're now in the middle of a large study for pediatric approval of the InfraScanner. Because when the FDA approved the device, they did not feel that we had enough kids in the study, so it was approved only for adults and now we are running a study to get it approved for kids; and the FDA is not making our life easy. And the same, by the way, is true in China. In China, the FDA is also pretty tough agency.

GREG SARIAN: **What is the greatest value brought to patients with the InfraScanner device?**

BARUCH BEN DOR: Timeliness—Time lost is brain lost. So the critical thing is to bring diagnosis to an environment that doesn't have that capability. It's really early triage or early diagnosis that the patient has brain bleeding greatly increase the chances of that patient surviving.

We had a case of an Afghan child that was near the Marines in Afghanistan when an IED went off, and he had a small scalp laceration. He was lucky that the Marines had the InfraScanner which showed that he had brain bleeding. Instead of sending him home with a band aid on this head, they evacuated him to Kandahar, and the neurosurgeon saved his life.

We had another case of a soldier that seemed to clinically stable, but InfraScanner showed that he had developed bleeding. He was evacuated although it was in the middle of a sand storm and normally helicopters are not sent out but based on the InfraScanner they knew he would not survive without evacuating him. Our product confirmed that he did have bleeding and immediately went into surgery and his life was saved.

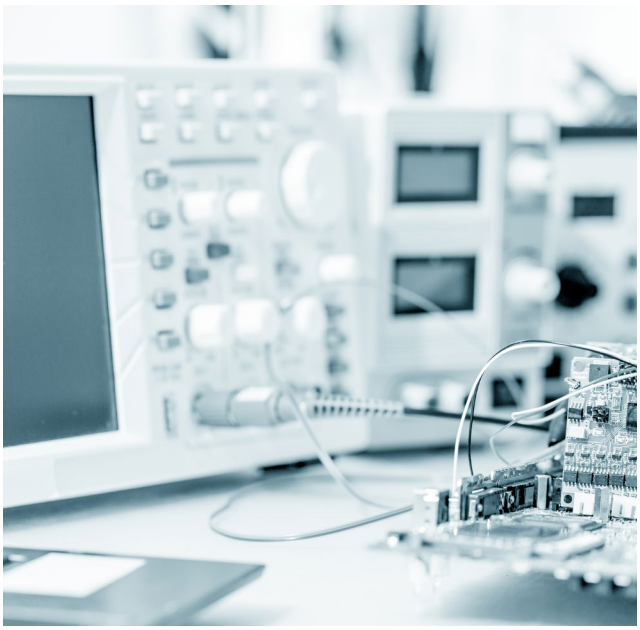
GREG SARIAN: **So what's the future like when you think three to five years out? What additional ways you're helping patients with the additional solutions are you bringing to the medical device industry?**

BARUCH BEN DOR: Our next generation product that we're developing is designed for en route care. U.S. Military medicine is now going through transformation where they realize that in the next conflict, wherever that will be, most probably U.S. will not have the air superiority it enjoyed in Iraq and Afghanistan and if a soldier is evacuated, the evacuation time will be much more than the ten minutes flight that was common in Iraq or Afghanistan. So now the focus is on en route care or devices and solutions that allow in a very limited environment as much care as possible—hoping the diagnosis should help both in triage, but most importantly through resuscitation effort as the patient is being evacuated.

GREG SARIAN: **What about your decision to remain in Philadelphia? You have headquarters in Downtown Philadelphia and we've seen a tremendous surge of device companies in the city. What's the main advantage or benefit for you in growing your business in the Greater Philadelphia region?**

BARUCH BEN DOR: Greater Philadelphia succeeded to create an ecosystem that is very favorable to Medtech companies is in Philadelphia. First of all and that's the most important thing, there is a very high level infrastructure of Universities in this area. So there is abundance of high level scientists and professional manpower coming from those universities—together with those universities there are world class hospitals that provide both the place to test and also provides the medical scientists that sometimes are key to developing or inventing those technologies.

Philadelphia, or the state of Pennsylvania in general, was very creative and very constructive in creating mechanism for early stage funding such as BioAdvance or Ben Franklin Technology Partners and even the City of Philadelphia through PIDC—Philadelphia Industrial Development Corporation is also supporting and early stage funding. So it's a phenomenal eco system both science and money and people.



THE PLANNING PRESCRIPTION: IMPORTANT MID YEAR PLANNING STRATEGIES

by Greg Sarian, CPWA® | CIMA® | CFP® | ChFC® | CEPA®
Managing Partner, The Sarian Group at HighTower

Throughout the summer and into early fall, tax and retirement planning may be the last thing on your mind. Our team always advises that mid-year is a strategic time to review some of your planning considerations. Assessing your position relative to your tax minimization and retirement goals—with enough time left in the year to make adjustments as necessary—gives you flexibility you may not otherwise have had.

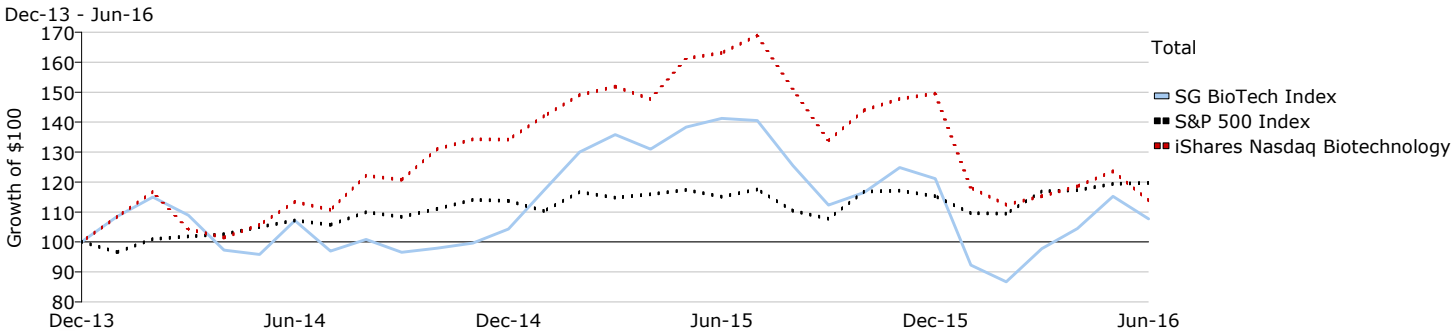
First, take a moment to look at your paystubs or distributions to determine if your tax withholdings are accurate. You may also want to review your position regarding realized and unrealized gains and losses. Sitting on unrealized losses may give you flexibility if you sell other securities at a gain during the rebalancing process. If you have variable compensation or corporate transactions, you may want to determine if you are falling into a higher marginal tax bracket. Deferring compensation or pushing a bonus to 2017 may defer or reduce your tax liability. Conversely, if you are experiencing a lower income year, you may want to consider converting a portion of your IRA into a Roth IRA. While the amount converted will be included on your 2016 taxable income, if it is left in for five years it will grow tax free and can be withdrawn with no tax liability after you have reached age 59.

If you are still working, also look at your paystub to determine whether or not you are maximizing your 401k contributions. Those under age 50 can defer up to $18,500 in a 401k, while those over age 50 can defer up to $23,500. If these thresholds are already exceeded, you can still save in after-tax accounts or non-deductible IRAs. For retirees over 70, review your position regarding required minimum distributions. Your IRA custodian can calculate your specific dollar amount and doing this mid-year gives you until December 31st to complete your withdrawal. In 2016, the charitable giving clause was re-enacted, so you can avoid the tax liability of the RMD if your withdrawal goes directly from your IRA to a qualified charity. No tax deduction is received, but there is no tax on the amount withdrawn. This may be advantageous for those retirees whose income sources are subject to phasing them out from the sum total of their itemized deductions. Finally, from a cash flow planning perspective, this is a great time to compare actual sources of inflow and outflow to your stated budget. At mid-year, discrepancies can be found and adjustments can be made for the remainder of the year.

Getting your financial plan on track at the mid-year provides you with opportunities to identify and correct any discrepancies that may have arisen during previous six months. Just a few minutes of review could help you meet your goals for the year. Please feel welcome to call or email our office with any questions.

THE SARIAN GROUP INDEX*

The Sarian Group Index started in January 2013 to track regionally located HealthCare oriented businesses whose stock is traded above $1 a share against the S&P 500 and the NASDAQ Biotechnology index. It is an equally weighted index of publicly traded life sciences companies headquartered in PA, NJ and DE and is rebalanced monthly. Below is a look at the performance pattern since December 2013 along with a list of the companies that are currently included. Also listed are the Top Ten Companies who have had the largest gains and losses YTD within the index.



PORTFOLIO HOLDINGS

Aclaris Therapeutics Inc	Egalet Corp	Onconova Therapeutics Inc	NPS Pharmaceuticals Inc
Agile Therapeutics Inc	Globus Medical Inc	PTC Therapeutics Inc	Aerie Pharmaceuticals Inc
Celator Pharmaceuticals Inc	Johnson & Johnson	TetraLogic Pharmaceuticals Corp	Cancer Genetics Inc
Echo Therapeutics Inc	Mylan NV	Auxilium Pharmaceuticals Inc	Eagle Pharmaceuticals Inc
GlaxoSmithKline PLC	ProPhase Labs Inc	Advaxis Inc	Fibrocell Science Inc
Insmed Inc	Spark Therapeutics Inc	Amicus Therapeutics Inc	Inovio Pharmaceuticals Inc
Merck & Co Inc	Active Control Technology Inc	Windtree Therapeutics Inc	The Medicines Co
PhotoMedex Inc	Alcobra Ltd	Enzon Pharmaceuticals Inc	Pacira Pharmaceuticals Inc
Safeguard Scientifics Inc	Alliqua BioMedical Inc	Incyte Corp	Recro Pharma Inc
Zynerba Pharmaceuticals Inc	Cyclacel Pharmaceuticals Inc	Medgenics Inc	Trevena Inc
Adaptimmune Therapeutics PLC	Endo International PLC	Ophthotech Corp	
Akers Biosciences Inc	Immunomedics Inc	Tobira Therapeutics Inc	
Celgene Corp	Lannett Co Inc	Vitae Pharmaceuticals Inc	

TOP TEN GAINERS — YTD 06/30/2016

Celator Pharmaceuticals Inc	1614.77	%
Akers Biosciences Inc	166.12	%
Inovio Pharmaceuticals Inc	37.50	%
Regado Biosciences Inc	24.98	%
Johnson & Johnson	19.77	%
Spark Therapeutics Inc	12.84	%
GlaxoSmithKline PLC	12.27	%
Merck & Co Inc	10.90	%
Medgenics Inc	-7.81	%
Echo Therapeutics Inc	-8.45	%

TOP TEN DECLINERS — YTD 06/30/2016

TetraLogic Pharmaceuticals Corporation	-82.3	%
PTC Therapeutics Inc	-78.33	%
Fibrocell Science Inc	-74.73	%
Endo International PLC	-74.53	%
Eagle Pharmaceuticals Inc	-56.25	%
Pacira Pharmaceuticals Inc	-56.08	%
Egalet Corp	-54.99	%
Alliqua Inc	-47.66	%
Insmed Inc	-45.67	%
PhotoMedex Inc	-43.98	%

*Information provided by the Markov Processes International LLC (MPI)

PHILLY FUNDINGS

RADIUS HEALTH

June 22—Radius Health Inc., a Massachusetts-based biopharmaceutical company developing new treatments for osteoporosis, oncology and endocrine diseases, has opened a 14,000-square-foot office in Wayne, Pa., where it plans to employ a staff of more than 100 workers. The site in the Crosspoint Office Park on Swedesford Road, will be the home of the commercial, pharmacovigilance and medical affairs teams for Radius, which is preparing for its potential first commercial product launch. The company's lead drug candidate is under review by the Food and Drug Administration as a potential treatment for postmenopausal women with osteoporosis.

1315 CAPITAL

June 15—1315 Capital, LLC, an expansion and growth equity firm that invests in commercial-stage specialty pharmaceutical, medical technology, and healthcare services companies, today announced the final closing of its $200 million inaugural fund. The fund is led by seasoned healthcare investors and 1315 Capital's Co-Founders, Adele Oliva and Michael Koby, and includes a select group of high quality investors, including endowments, foundations, state and corporate pension funds, and family offices.

FREENOME

June 13—Freenome, a company started by a former University of Pennsylvania doctoral student that is developing a software-enable liquid biopsy test to detect cancer in its earliest stages – has raised $5.5 million in a private stock sale led by Andreessen Horowitz. Andreessen Horowitz is a Silicon Valley-based venture capital firm that recently established a $200 million biotech fund. Freenome recently moved its corporate headquarters to Palo Alto, California from Philadelphia. It will continue to maintain operations in Philadelphia.

PENNSYLVANIA BIO

SAVE THE DATE | PEER TO PEER BREAKFAST

SPONSORED BY THE LIFE SCIENCE EXECUTIVE NETWORK AT THE SARIAN GROUP AT HIGHTOWER

Date & Time: Friday November 11, 2016 | Breakfast will be served at 7:45 a.m.
Location: Crowne Plaza Philadelphia—King of Prussia | 206 Mall Blvd, King of Prussia, PA 19406
Topic: Rare Disease: What are the Keys to Sustainable Progress?