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The Georgia Bio Industry E-Newsletter

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Letter from the President: New Directions for 2017

As we close out another year at Georgia Bio, we are gearing up for the Georgia Bio Awards Dinner. The Georgia Bio Life Science Luminaries Gala Celebration & Awards Ceremony will take place Thursday, January 26, 20167 at the Westin Atlanta Perimeter. The event is a celebration of the contribution and achievements of Georgia bioscience and medtech leaders, and provides a moment to pause and reflect on the industry's legacy. This year we are excited to roll out a new name, look and venue for the dinner. Sponsorships are available and the event is sure to be a sell out!

Additionally, in 2017 I am pleased to introduce some of the new initiatives we plan to take for benefit of the industry. Be on the lookout for more information, but you are always welcome to reach out to us if you have interest in further involvement or if you would like to explore your member benefits.

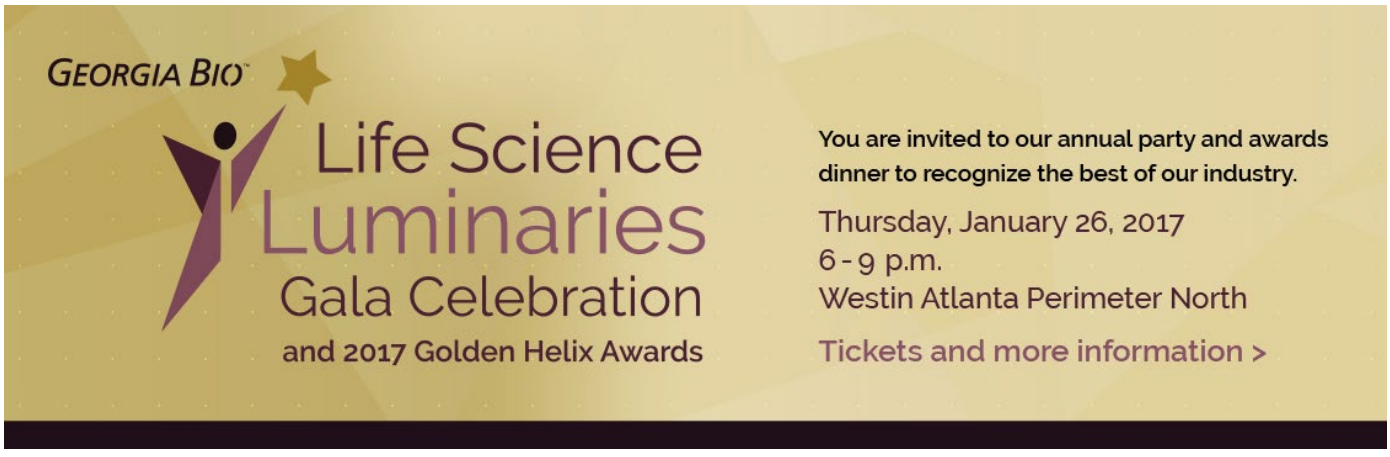
- Robust calendar of events with over 30 programs anticipated in 2017, produced in partnership with our committees & networks
- New structure and charters for our committees and networks to better serve all sectors of our membership
- Quarterly membership meeting & networking program
- Creation of an online industry resource clearinghouse

In addition to these activities, we are exploring enhancements to our Summit, Awards Dinner and other major events. Our primary goal is to help you grow your business, build your future workforce, make connections and thrive in Georgia. Please let us know what we can do to help you.

I thank you for your involvement and assistance with our mission and look forward to seeing you in 2017!

Thank you,

Russell Allen
President & CEO
Georgia Bio



Cybersecurity Risks to Medical Devices

Deciding When to Submit a 510(k) for a Software Change to an Existing Device

Datalynx

During a "60 Minutes" interview, former US Vice President States Dick Cheney revealed that his doctor ordered the wireless functionality of his pacemaker be disabled due to fears it might be hacked in an assassination attempt.[2] Sergey Lozhkin, a senior researcher at security firm Kaspersky Lab, details how he was able to hack into a hospital's Wifi network with ease and find thousands of hospital devices online using Shodan (internet search engine to identify networked devices).[1] Lozhkin warns, "If you know, for example, what feedback an MRI or laser or cardiology device gives when you connect to its port, you can go to Shodan and find hundreds of these devices, and if you know a vulnerability you can hack all of them."[1]

As more medical devices become connected to the internet, hackers are a rising concern.[1] Attacks against medical devices expose not only reams of patient data, but also access to MRI devices, x-ray machines, drug infusion pumps, and management applications; that could lead to catastrophic results if they are reconfigured by an attacker.[1] Researchers have also exposed vulnerabilities in internet-connected implanted medical devices, which pose a large health risk for the public.[1] Protecting against "medical cybercrime" is difficult, as most medical manufacturers find it challenging to acquire the tools and expertise needed to address vulnerabilities in medical devices.[1,5]

The FDA recommends that medical device companies follow the cybersecurity principles "Identify, Protect, Detect, Respond, and Recover" to guide their cybersecurity activities.[1] Over the life of the medical device, manufacturers may come across device vulnerability to security hacks, forcing them to update the software and ensure security of the device.[1,3] Cybersecurity updates are considered a subset of software changes implemented to strengthen the security of a system, protect information, and reduce disruption in service. FDA expects manufacturers to ensure that such changes do not impact the performance or the functionality of the device by conducting necessary analysis, verification, and/or validation.[3] In many cases, a change made solely to strengthen cybersecurity may not require a new 510(k).[1,3] However, if a manufacturer becomes aware of any incidental or unintended impacts of the change on other aspects of the software or device, they must submit a premarket notification.[3]

The regulatory criteria in ESTABLISHMENT REGISTRATION AND DEVICE LISTING FOR MANUFACTURERS AND INITIAL IMPORTERS OF DEVICES – "21 CFR 807.81(a)(3)" states that a premarket notification must be submitted when:[4]

- The device is one that the person currently has in commercial distribution or is reintroducing into commercial distribution, but that is about to be significantly changed or modified in design, components, method of manufacture, or intended use. The following constitute significant changes or modifications that require a premarket notification:
    - o A change or modification in the device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process.
    - o A major change or modification in the intended use of the device.[4]

Clarification of Cybersecurity & Software Changes to Medical Device

In the past, there has been ambiguity if these security updates and/or changes to medical devices require resubmission for 510(k) approval. Thus, in August 2016, the FDA published a guidance document, titled "Deciding When to Submit a 510(k) for a Software Change to an Existing Device," which assists industry and regulatory staff in determining when a software change (to an existing device) may require a manufacturer to submit a new premarket notification.[3] This guidance document along with "Content of Premarket Submissions for Management of Cybersecurity in Medical

Devices" issued on Oct 2 2014, helps manufacturers identify and address issues related to cybersecurity, as well as prepare premarket submissions for applicable devices.[3]

The guidance document, "Deciding When to Submit a 510(k) for a Software Change to an Existing Device," covers the following:[3]

- Modifications made with intent to significantly affect safety or effectiveness of a device
- "Could significantly affect" evaluation and the role of testing
- Unintended consequences of changes
- Use of risk management
- Evaluating simultaneous changes
- Appropriate comparative device and cumulative effect of changes
- 510(k) submissions for modified devices
- Substantial equivalence determinations

When finalized, the guidance document, "Deciding When to Submit a 510(k) for a Software Change to an Existing Device," will further assist industry and agency staff in determining when a software (including firmware) change to an existing device (510(k)-cleared) may require a manufacturer to submit and obtain additional FDA clearance of a new premarket notification (510(k)).[3]

How Datalynx Can Help You Bridge the Gap to Compliance

With 20 years of experience in regulatory compliance, Datalynx is poised to help you through the process of determining if the software changes made to a medical device require a 510(k) submission. We can help at any stage of the process by ensuring the proper support is present to bring your team up to speed and meet the requirements of the FDA mandate.

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References

1Brook, C. (2016, February 18). Sergey Lozhkin on How He Hacked His Hospital. Retrieved August 11, 2016, from https://threatpost.com/sergey-lozhkin-on-how-he-hacked-his-hospital/116314/

2Gupta, S. (2013, October 20). Dick Cheney's Heart. Retrieved August 11, 2016, from http://www.cbsnews.com/news/dick-cheneys-heart/

3United States of America, Food & Drug Administration, Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER). (2016). Deciding When to Submit a 510(k) for a Software Change to an Existing Device (pp. 1-32). US Dept. of Health & Human Services

4United States of America, Food & Drug Administration. (2015). Code of Federal Regulations Title 21 (Vol. 8). Silver Spring, MD: US Dept. of Health & Human Services.

5Wadhwa, T. (2012, December 12). Yes, You Can Hack a Pacemaker. Retrieved August 11, 2016, from http://www.forbes.com/sites/singularity/2012/12/06/yes-you-can-hack-a-pacemaker-and-other-medical-devices-too/#56e3129513e0

Cancer Vaccines and Game Changers

By Emily Burke, BioTech Primer

THE ELUSIVE CANCER VACCINE

The promise of cancer vaccines has proven to be elusive. A new crop of biotechs is hoping to change that by taking advantage of the latest advances in genomics. Scientists are working overtime trying to develop cancer vaccines that train the immune system to recognize and fight an established tumor. In this WEEKLY, we'll break down the science and technology of immunotherapeutic vaccines.

TERM OF THE WEEK: NEOANTIGEN

An antigen is a protein or portion of a protein present in a cell that is recognized by the immune system. Think of antigens as flags; some flags are "good" and some flags are "bad." An immune response occurs when attack cells, such as macrophages and cytotoxic T-cells, encounter a "bad" flag. The best case scenario: cells waving the "bad" flag or antigen are recognized, targeted and killed. Worst case scenario: cells waving the "bad" flag or antigen have evolved strategies to operate in stealth mode. This cloaking mechanism is often used by cancer — it is the reason why it can be a silent disease until the very late stages.

As a tumor grows, it can accumulate additional mutations (changes in the DNA). Scientists have found some of these mutations are significant enough to produce new antigens that the immune system can recognize. These are called neoantigens, and they are the secret sauce in cancer vaccines.

FINDING NEOANTIGENS

One of the hallmarks of cancer cell development is a high rate of DNA mutation. Once a tumor is established, it may grow to have dozens or even hundreds of mutations that differentiate it from healthy cells. Identifying these cancer mutations begins with performing a biopsy to collect and study a small sample of tumor cells. Thanks to advances in genome sequencing technology, researchers can sequence the tumors entire "exome," the portion of the DNA used to make proteins. Since only the exome is used to produce antigens, scientists look only at the exome to identify neoantigens. Tumor cell exomes are then compared to healthy cell exomes, and the differences in DNA sequences are identified.

It turns out not all proteins make good antigens; the best are those displayed on the cell surface where they can be recognized by the immune system. In order to identify cell surface neoantigens, the "unique to cancer DNA sequences" are fed into bioinformatics programs that predict the probability of surface location. Typically around 5% of the mutated genes are potential neoantigens.

TRAINING THE VACCINE

Once neoantigens are identified, they are synthesized in the lab and mixed with an adjuvant, a substance that boosts the overall immune response. Ideally, a neoantigen-based vaccine contains at least twenty different neoantigens, both to produce a strong immune response and reduce the likelihood of resistance. A tumor may mutate and stop producing one neoantigen, but it is unlikely to stop producing several simultaneously.

Although in some cases, several different patients may share common neoantigens, others may be unique to a given patient. So it is likely that these types of cancer vaccines would be truly personalized medicine — designed just for one patient. This type of precision was unimaginable even just a few years ago, but is possible today because of the increased efficiencies in both time and money achieved with genome sequencing.

THE GAME CHANGERS

Several neoantigen-based vaccines are already in clinical testing. Currently, the time taken to identify neoantigens and produce a vaccine is around six to twelve weeks; the goal is to bring this development time down to one month. Key players include:

- **TapImmune** (Jacksonville, FL) began Phase II clinical studies for a neoantigen-based vaccine (TPIV 200) for triple-negative breast cancer, the most difficult type of breast cancer to treat using today's therapies. TPIV 200 will be tested in combination with AstraZeneca's (London, UK) durvalumab, a checkpoint inhibitor currently in Phase III clinical testing.
- **Neon Therapeutics** (Cambridge, MA) is testing its melanoma and glioblastoma neoantigen vaccine, NEO-PV-01, in Phase Ib clinical studies in combination with **Bristol-Myers Squibb's** (New York, NY) already approved checkpoint inhibitor therapy Opdivo.
- **Gritstone Oncology** (Emeryville, CA) and **Immune Design** (Seattle, WA) have a partnership to discover and develop neoantigen-based vaccines, with clinical trials for a non-small cell lung cancer product expected to begin in 2017. Patients in the trial will be treated with a neoantigen vaccine in combination with an as yet unnamed immune-checkpoint inhibitor. Checkpoint inhibitor treatments relieve the natural inhibitions on cytotoxic T-cells, enabling the immune system to become fully activated in response to the vaccine.

If any of these companies succeed, we will be witness to truly personalized medicine at work.

Top Takeaways From the 2016 GaBio Summit

By Kristin Lindsey, Sr. Marketing Director, Curant Health

Every year, biotech industry leaders throughout the southeastern United States convene at Georgia Bio's flagship conference. Georgia Bio Summit 2016 was no different as hundreds of professionals representing pharmaceutical manufacturers, patient advocacy groups, innovative growth stage companies, service providers and academic institutions met at the Cobb Galleria Center on September 28th.

Gatherings like the Georgia Bio Summit provide the opportunity for healthcare thought leaders to share varying perspectives, a critical precursor in the development of a common vision of value across stakeholders.

In case you were not able to attend, here are a few of our top takeaways from #GaBioSummit.

THE PHARMACEUTICAL MANUFACTURER VIEW: SHIFTING PERCEPTION AND SOLVING FOR VALUE IS GOING TO TAKE A VILLAGE

Jim Greenwood, President & CEO of the Bio Industry Organization, delivered a breakfast keynote which he outlined the industry's ability to deliver value, including areas of healthcare spending increasing faster than pharma. He highlighted a new advertising campaign and web property dubbed "Innovation Saves" intended to change the public's current perception of the pharmaceutical industry.

It's true. Pharmaceutical manufacturers are doing wondrous work bringing not just new therapies, but cures for chronic illnesses like hepatitis C, to market. These therapies are capable of reducing overall healthcare costs and improving the lives of millions of patients worldwide. In his own words, essentially similar to those he delivered to Forbes last month, "What patients notice is what comes out of their pockets. That's not up to us—it's up to the insurance companies. If a cancer drug costs $100,000 and an insurer imposes a 30% co-insurance, the patient has to find $30,000. The patient doesn't have $30,000. Say that price is cut in half. The patient now has to find $15,000. And it might as well be $30,000. People aren't sitting around with $15,000 in their wallets. We cut our price by two-thirds, and they're still paying $10,000.

"So we can't unilaterally remove the burden from the patient. Insurance companies can. Regardless of whether we cut our price by 50% or two-thirds, innovation will be over."

We know the shift to value-based care will be challenging for every member of the ecosystem, including providers, patients, payers and manufacturers. A successful outcome of this shift is predicated on improved stakeholder alignment. We see the results of successful, value-based collaboration every day through our patient support services, medication management programs and our partner organizations.

THE PATIENT VOICE: BREAKING DOWN SILOS BETWEEN INDUSTRY AND PATIENTS

To provide the patient perspective, the Georgia Bio 2016 programming committee convened a lunch keynote led by Jesse Milan, Jr., JD, Interim President & CEO, AIDS United.

Jesse told an impassioned story about how he recently celebrated his 60th birthday. In no small part due to the phenomenal advancements in science brought by the pharmaceutical industry, Jesse has been living with HIV for 30 years. [Related – Curant Health's medication therapy management programs and patient support services are proven to improve outcomes and reduce costs for HIV patients.]

Jesse then invited Andy Lipman, author and member of the board of directors of the Cystic Fibrosis Foundation, and Suz Schrandt, JD, director of patient engagement for the Arthritis Foundation, to join him. At the age of 38, Andy passed the current median life expectancy for people with Cystic Fibrosis. Andy is now 42 years old. Suz was diagnosed with rheumatic disease at age 14.

GETTING TO VALUE: TYING ECONOMIC MEASURES TO CLINICAL STUDIES WILL BE KEY TO VALUE-BASED DEVELOPMENT AND COMMERCIALIZATION

During the afternoon breakout session focused on value derivation, Jake Caines, Director of Commercial Strategy for Curant Health, suggested that economic metrics are a 'must do' when it comes to clinical trials and studies. In the ACA era, if a new pharmaceutical therapy, healthcare service or device is not able to improve both factors of the value equation — outcomes divided by costs — it will be severely handicapped in its commercial success.

We eagerly await the results of value-based studies and analyses on which we are working with pharmaceutical manufacturers and provider partners including Johns Hopkins, Northwestern University and others.

We would like to thank Georgia Bio for its continued leadership and commitment to the advancement of our regional bioscience and medtech community. The Curant Health team was honored to be invited to share insights on the definition of "value," the price of innovation, implementing outcomes-based reimbursement, the impact of health policies on behavior and the relationship between price and cost of all facets of healthcare delivery.

If you'd like to know more about what's needed to derive the greatest value from specialty pharmaceuticals for chronically ill patients on complex regimens, contact Senior Director of Marketing, Kristin Lindsey, at klindsey@curanthealth.com or call 866-437-8040.

We look forward to Georgia Bio Summit 2017! View more Georgia Bio Summit highlights here.

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For more than 15 years, VWR and BIO, the world's largest biotechnology trade association, have combined their core strengths to offer solutions that advance scientific innovation in the life sciences. Together, VWR and BIO provide the industry substantial cost savings and service solutions to accelerate science from discovery to production. Extend your purchasing power today.

Featured New Member: Intent Solutions, Inc.

Intent Solutions™ is a B2B technology, software, and data service company focused on developing solutions for clinical research, pain management and specialized pharmacy, designed to markedly improve the monitoring and management of medication adherence and providing real-time behavioral data to more accurately measure compliance and efficacy.

Our technology is designed to reduce the cost of health care, improve health care outcomes, and prevent the misuse, abuse, and diversion of prescription medications. We believe our technology is the next logical advancement in the way prescription medications are managed by both consumers and professionals.

Learn more here.

Welcome New Members

Applied Economics LLC

DRG Laboratory

Intent Solutions, Inc.

Kiel Laboratories, Inc.

Silver Legal & Compliance Special Ops, LLC

Thermo Fisher Scientific

Upcoming Events

Careers in Life Sciences Series: Entrepreneurship
December 1, 2016

The SEBIO Investor & Partnering Forum
December 11-12, 2016

Biotech Showcase 2017
January 9-11, 2017

Georgia Bio Life Science Luminaries Gala Celebration
January 26, 2017

2nd Annual Biomarker Conference
February 6-7, 2017

2nd Annual Genome Editing & Engineering Conference
February 6-7, 2017

Data Integrity -
What Data Does When No One's Looking
February 17, 2017

BIO Legislative Day Fly-in
April 4-5, 2017

World Orphan Drug Congress USA 2017
April 19-21, 2017

2017 Georgia Logistics Summit
May 16-17, 2017

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