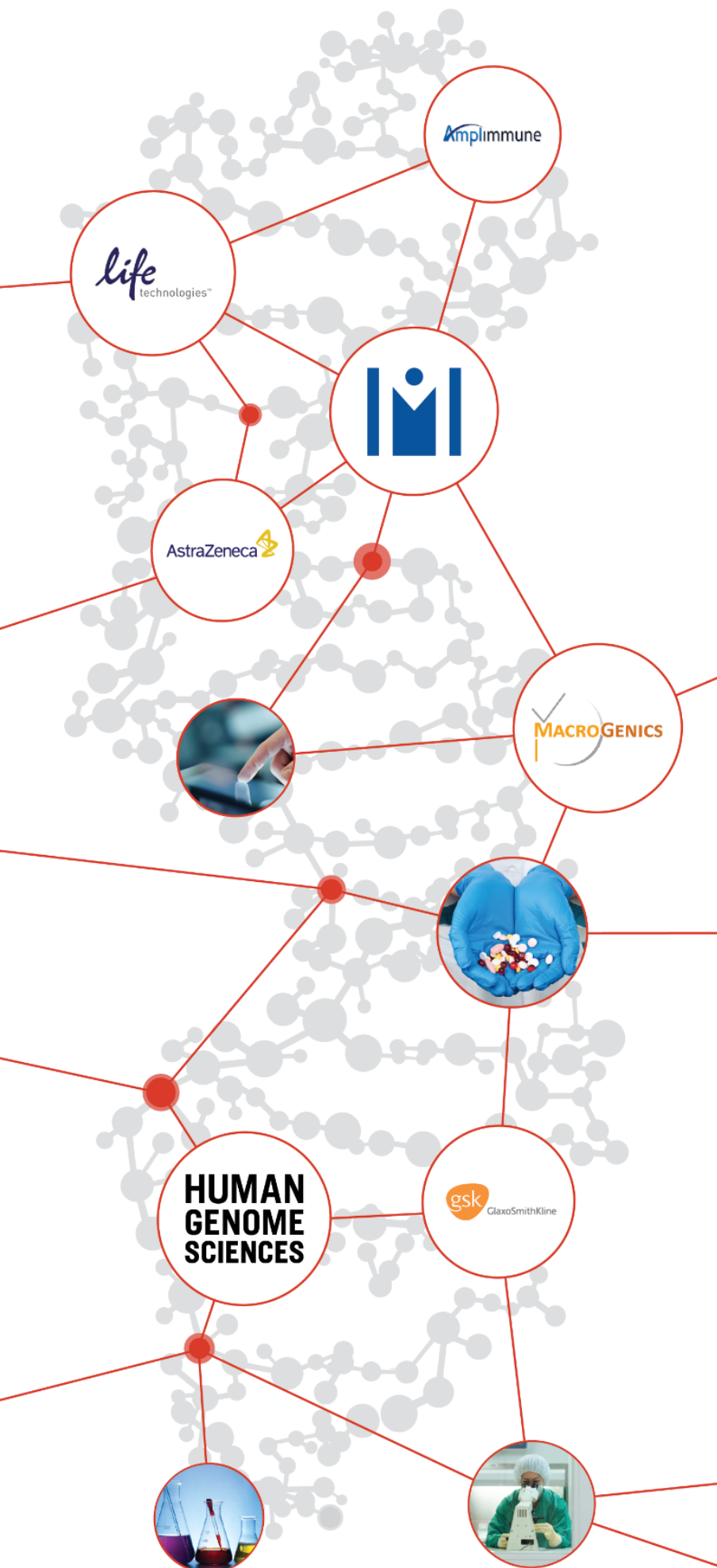


# Updated Genealogies of Central Maryland BioHealth Companies

*A Report to the  
Economic Alliance of Greater  
Baltimore and  
BioHealth Innovation*

MRBS LLC  
2015





## Acknowledgements



**The Economic Alliance of Greater Baltimore** is a not-for-profit economic development organization led by a partnership of regional business executives, elected government officials and leaders from higher education focused on fostering business retention and development, job creation, workforce development and new investment throughout the Greater Baltimore region. The region is defined as Baltimore City and its seven surrounding counties: Anne Arundel County, Baltimore County, Carroll County, Cecil County, Harford County, Howard County and Queen Anne's County.



**BioHealth Innovation, Inc.** is a regional innovation intermediary that accelerates and facilitates technology transfer and commercialization of market-relevant research in federal labs, universities, and biohealth companies in the Region. It is a private-public partnership in the form of a 501 (c)(3) nonprofit that connects the Region's innovation assets to provide integrated technical knowledge, financial means and entrepreneurial/managerial expertise to turn promise into prosperity for the region while advancing human health.



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# Updated Genealogies of Central Maryland BioHealth Companies: Findings and Analysis of Updated Information

**Report Background:** As the 21st century dawned, Maryland Technology Development (TEDCO) and the Maryland Department of Business and Economic Development (DBED) commissioned a set of studies – published in 2002 and 2004 – of the “genealogies,” or family histories, of companies in the bioscience, medical instruments, and bio/medical/health informatics sectors.<sup>1</sup> Marsha Schachtel, current Principal of MRBS LLC, and her graduate student research assistants at the Johns Hopkins Institute for Policy studies undertook the work. This report summarizes an analysis of a recent update by MRBS LLC of these inventories.

**Summary:** At the midpoint of the second decade of the 21<sup>st</sup> Century, the seed corn in Maryland’s research institutions remains at healthy levels. The rates at which it has been drawn down and planted and nurtured successfully have accelerated. The investments in new eco-friendly fertilizers such as mentors and growth accelerators have paid off. The new crop of biohealth companies is thriving.

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## I. Introduction

The “genealogies” of Maryland technology companies are intertwined stories of entrepreneurs, technologies, and corporate dynamics. This update describes firms that have emerged out of the State’s own unparalleled set of research institutions or their founders’ own ingenuity, have grown or shrunk, moved out of or into the State of Maryland, or merged or spun off other firms. It also clearly illustrates the successive generations of technology development in core fields like vaccines, genomics, medical devices, and the productive integration of information technologies and engineering into bioresearch, medicine, and health care. Firms that use bioscience for purposes other than direct impacts on human health – agriculture, environmental protection and restoration, food, industrial processes, nutraceutical, and veterinary – have also been included.

BioMaryland, Montgomery County, news sources, commercial databases, and MRBS LLC files provided the sources for initial lists of companies, which were winnowed down to eliminate duplicates, change names where appropriate, and remove companies known to be out of business or out of Maryland. Approximately 700 companies remained and were analyzed, adding information wherever possible to

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<sup>1</sup> Electronic copies may be requested from Maryland TEDCO ([tedco.md](http://tedco.md)) or MRBS LLC ([mschachtel@comcast.net](mailto:mschachtel@comcast.net))

flesh out profiles in the inventory. The master list does not include management consulting other than for start-ups; facilities; federal enterprise and program management IT; health enterprise IT, pharmacy management, coding, health care claims and payments, or other related healthcare business-related IT.

Approximately 80 of the roughly 300 bioscience companies inventoried in 2002 continue in operation in Maryland, either under their original names or those of the companies that acquired them. There are 44 public biohealth companies presently operating in the State. In addition, there are 10 companies that are business units of other U.S. public companies, and 24 companies that are business units of foreign public companies, many of them CROs. The latter are headquartered across the world, in Canada, Denmark, France, Germany, India, Ireland, Israel, Japan, Korea, Netherlands, Scotland (UK), and Switzerland.

**Table 1. Public Biotechnology and Life Sciences founded in Maryland**

| Company Name   | Year Founded | IPO Year | Ticker or Current Status            |
|--|--------------|----------|-------------------------------------|
| Rexenxbio, Inc.  | 2009         | 2015     | NASDAQ: RGNX                        |
| GlycoMimetics, Inc.  | 2003         | 2014     | NASDAQ: GLYC                        |
| Vanda Pharmaceuticals, Inc.                                  | 2002         | 2006     | NASDAQ: VNDA                        |
| OpGen Technologies, Inc.                                     | 2002         | 2015     | NASDAQ: OPGN                        |
| PharmAthene, Inc.  | 2001         | 2005     | NYSE MKT: PIP                       |
| Rexahn Pharmaceuticals, Inc.                                 | 2001         | 2005     | NYSE MKT: RNN                       |
| BioElectronics Corp.   | 2000         | 2008     | OTCMKTS: BIEL                       |
| MacroGenics, Inc.  | 2000         | 2010     | NASDAQ: MGNX                        |
| Advancis Pharmaceuticals Corp. (MiddleBrook Pharmaceuticals) | 1999         | 2003     | Not operating                       |
| Avalon Pharmaceuticals, Inc.                                 | 1999         | 2005     | Not operating                       |
| Emergent BioSolutions Inc.                                   | 1998         | 2006     | NYSE: EBS                           |
| Intrexon Corp.   | 1998         | 2013     | NYSE: XON                           |
| Northwest Biotherapeutics, Inc.                              | 1998         | 2001     | NASDAQ: NWBO                        |
| Iomai Corp.  | 1997         | 2006     | Acquired by Intercell AG in 2008    |
| Neuralstem, Inc.   | 1996         | 2006     | NYSE MKT: CUR                       |
| Sucampo Pharmaceuticals, Inc.                                | 1996         | 2007     | NASDAQ: SCMP                        |
| United Therapeutics Corp.                                    | 1996         | 1999     | NASDAQ: UTHR                        |
| Gene Logic, Inc. (Ocimum)                                    | 1994         | 1997     | Not operating                       |
| GenVec, Inc.   | 1992         | 2000     | NASDAQ: GNVC                        |
| Human Genome Sciences, Inc.                                  | 1992         | 1993     | Acquired by GlaxoSmithKline in 2012 |
| Osiris Therapeutics, Inc.                                    | 1992         | 2006     | NASDAQ: OSIR                        |
| CASI Pharmaceuticals, Inc. (Entremed)                        | 1991         | 1996     | NASDAQ: CASI                        |
| Supernus Pharmaceuticals                                     | 1990         | 2012     | NASDAQ: SUPN                        |
| MedImmune, Inc.  | 1987         | 1991     | Acquired by AstraZeneca in 2007     |
| Novavax, Inc.  | 1987         | 1995     | NASDAQ: NVAX                        |
| Nuo Therapeutics, Inc. (Cytomedix)                           | 1987         | 2003     | OTC: NUOT                           |
| RegeneRx Biopharmaceuticals, Inc.                            | 1982         | 2010     | OTC: RGRX                           |
| BIOQUAL, Inc.  | 1981         | 1986     | OTCMKTS: BIOQ                       |
| Igene Biotechnology Inc.                                     | 1981         | 1986     | OTC US: IGNE                        |
| BioReliance Corp.  | 1947         | 1997     | Acquired by Sigma Aldrich in 2012   |
| W.R. Grace & Co.   | 1832         | 1953     | NYSE: GRA                           |

Maryland's human capital, particularly people with corporate experience, has broadened and deepened. The rate that technology changes, frequently fueled by information technology and engineering advances, has accelerated. Contextual changes in regulation and health care financing, world events

that have redefined threats, and heightened privacy and security concerns continue to create opportunities for biohealth companies.

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## II. Summary Conclusions and Commentary

In the time since the original bioscience companies inventory was completed in 2002:

- The number of biohealth companies has grown, although changing definitions of which companies meet the definitions for inclusion have changed, making it impossible to make precise comparisons.
- There are more big companies today and the good news is that transactions for the largest two, MedImmune (Astra Zeneca) and Human Genome Sciences (GlaxoSmithKline), did not cost Maryland bodies but rather increased investment in the state.
- Maryland now has the cadre of experienced entrepreneurs and managers it lacked in the early part of the decade. They not only continue to innovate and, in many cases, to create new businesses, but also provide a valuable source of business, science, and commercialization expertise for young companies that have followed them.
- The convergence of technologies finds Maryland in an ideal position. Its historical strengths in biotechnology are matched by deep IT systems and engineering strengths in industry and academia. Bioengineering is the largest undergraduate major at Johns Hopkins and the University of Maryland's Fischell Department of Bioengineering, launched in 2005, is already experiencing success. The Department's benefactor, Robert Fischell, is not only a satellite scientist but also a bio-entrepreneur, the father of medical stents and the founder of numerous bioengineering companies. The latter include Neuralieve (now eNeura and located in the University of Maryland BioPark), which is developing a magnetic pulse device that stops migraine headaches.
- Fischell joins an esteemed group of Maryland bio-pioneers, individuals who founded not only companies, but also whole new fields. In 1987, Jim Barrett founded Genetic Therapy with Dr. French Anderson, who headed a team of National Institutes of Health researchers that had developed a method to genetically alter human cells outside the body so they would provide therapeutic benefits against disease and disorders once placed back into patients. The company was sold in 1995 for \$295 million to Swiss pharmaceutical giant Sandoz AG. Jim Burns brought Osiris, one of the early stem cell companies, to Baltimore in 1992.
- Maryland companies continue to be focused on cutting edge science, often working at the earliest stages to bring it from laboratory to the market and medical practice.
- Spawned and still supported by the Army's medical research facilities in the state, Maryland's vaccine sector has blossomed to make it one of the largest clusters in the world.
- Universities continue to play a pivotal role, more frequently now as collaborators in advancing the commercialization of technologies in addition to serving as sources of basic discovery. The sea change – starting with the institutions' presidents – regarding commercialization at not only University of Maryland, a land grant institution, but also the last bastion of the ivory tower,

Johns Hopkins, has been dramatic. Both now employ managers with hands-on experience in private sector technology entrepreneurship and venture capital.

- The environment for bio-entrepreneurship has vastly improved since the beginning of the 21<sup>st</sup> century, increasing the survival odds for startups in this challenging sector. Experienced managers and advisors and an amped-up interwoven infrastructure of support help guide and sustain the newbies. Even the young companies today appear to be much savvier about how to get the help they need.
- Shortages of early stage funding continue to hamper promising companies, particularly as they grow in number and finance-readiness. The state's programs have been improved by managers who understand the sector and the levels and types of financing that make sense at various stages of development. The old days of \$25,000 grants have passed without mourning, and the programs have morphed to stay in tune with new regulatory/investor requirements and healthcare realities. For example, the BioMaryland Center, part of the Maryland Department of Business and Economic Development, announced earlier this year that it had put together a \$1 million challenge to biohealth entrepreneurs. The announcement read:

*As a result of ongoing payment reforms in Maryland being implemented under a waiver from Medicare, hospitals now will be rewarded for increasing the value rather than the volume of health care services, and for improving population health. This is creating an urgent need and compelling business case for the development of new health care technologies and services with the potential to improve patient outcomes while reducing overall health care spending. Therefore, for FY2015, the BioMaryland Center, in partnership with the Department of Health and Mental Hygiene (DHMH) and the Center for Medical Technology Policy (CMTP), mounted a \$1 Million Challenge to fund projects, \$50,000-200,000, focused on breakthrough innovations that both improve quality and reduce costs.<sup>2</sup>*

A dynamic set of new and experienced companies, entrepreneurs, and managers, along with a fast-maturing infrastructure of support for start-ups augur well for the State of Maryland's continued leadership in biohealth industries.

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## III. Human capital changes over the decade

### A. Pillar bioscience companies

Pillar bioscience companies that were young 15 years ago now supply management talent and new seasoned entrepreneurs. Maryland economic development professionals formerly bemoaned the scant supply of bioscience managerial talent in the state, especially when compared to New Jersey and Pennsylvania, in which large pharmaceutical companies or their U.S. headquarters, are located. But

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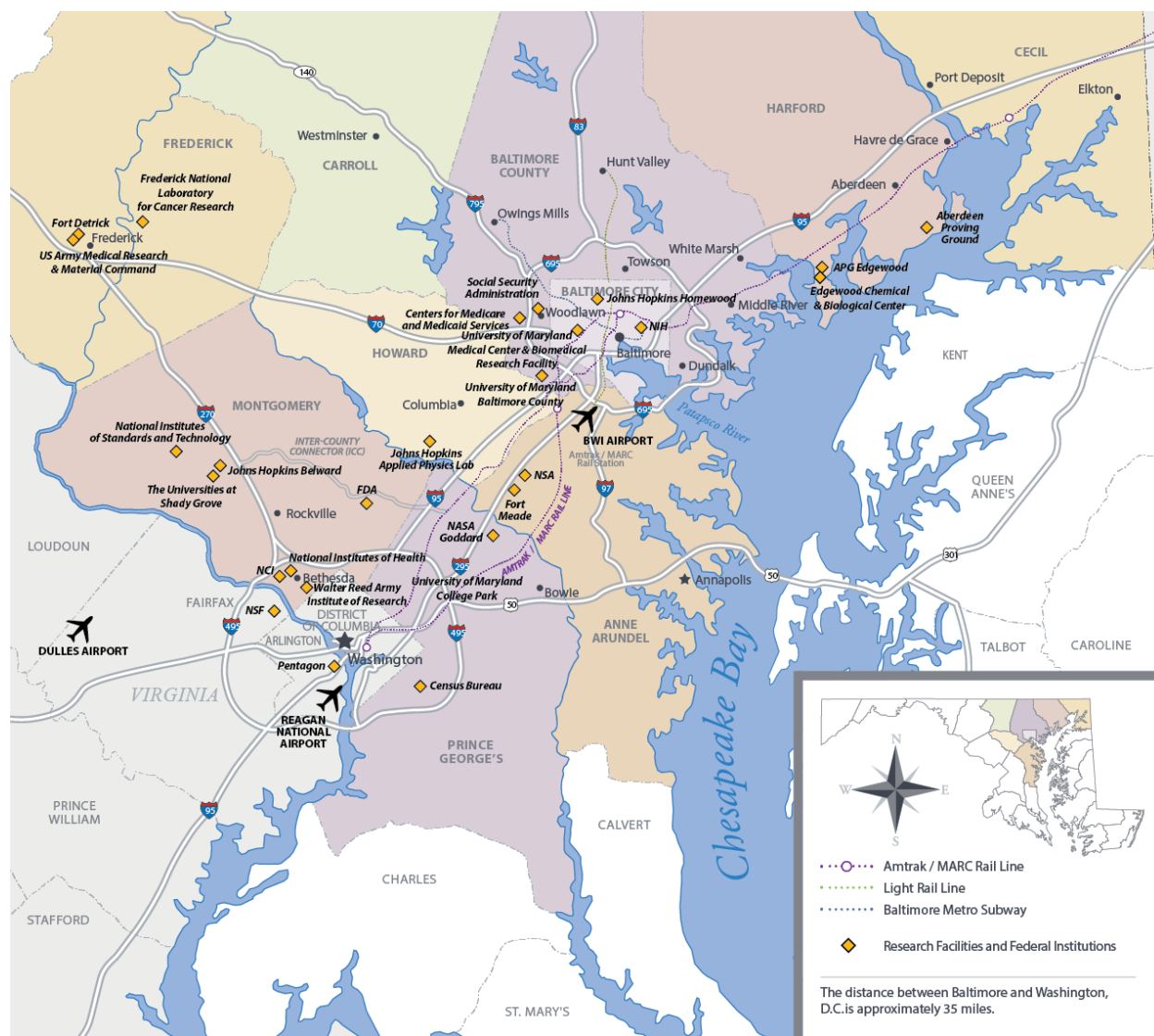
<sup>2</sup> <http://www.bio.maryland.gov/funding/pages/biotechnology-development-awards.aspx>



Maryland's bio-economy evolved from its particular science foundations, trending toward the use of living organisms or biological substances (biologicals) rather than biochemistry. The companies that grew large here were in the biotechnology industry, producing the "seed corn" of research and development services (Life Technologies) as well as vaccines (MedImmune) and genomics-based therapeutics (Human Genome Sciences.) Alumni of these companies, not just the founders, have not only started new companies in the state, but also become managers, board members, and advisors for many others, particularly as the latter enter the commercial phase. A number of the alumni have joined or inaugurated their own venture financing entities.

**An illustrative sampling from three pillar companies that have prospered in Central Maryland is presented on the following pages.**

### *Central Maryland's Unique Biohealth assets*





Life Technologies was founded in 1983 by the merger of Bethesda Research Laboratories, Inc. and GIBCO Corporation. Following much commercial success, Life Technologies was bought out by Invitrogen in 2000. After Invitrogen Corporation's acquired Applied Biosystems Inc., Invitrogen renamed itself as Life Technologies Corp. In 2014, Life Technologies became the fourth brand within Thermo Fisher.

**Table 2. Life Technologies**

| Former Life Technologies Employees (position)                        | Former Life Technologies Employees: Subsequent jobs   | M. James Barrett, Life Technologies Founder & CEO   |
|--|---|---|
| Robert Bebee   | <b>Molecular Transfer</b> , <sup>3</sup> Dir Mfg & Ops  | Previously employed in various divisions at SmithKline and President & CEO of <b>Bethesda Research Labs</b> (progenitor of Life Technologies)<br><b>Genetic Therapy</b> * (acq'd by Novartis), Founder See <b>INSERT</b> below<br>Sensors for Medicine & Science (now <b>Senseonics</b> ), Founder & director<br><b>MedImmune</b> (acq'd by AstraZeneca)                |
| Arthur "Skip" Colvin, Staff Scientist                                | Sensors for Medicine & Science (became <b>Senseonics</b> ): Scientific founder and source of IP<br><b>Twistnostics</b> , Advisor<br><b>Scanogen</b> , Advisor |   |
| Doug Doerfler  | <b>MaxCyte</b> , CEO  |   |
| Bill Enright, Manager of Licensing                                   | <b>Genvec</b> , Head of bus. devt<br><b>Vaxin</b> , President & CEO   |   |
| Guililat Gebeyehu, Dir R&D   | <b>Molecular Transfer</b> , EVP   |   |
| Christian E Gruber, developer of cDNA synthesis & cloning technology | <b>Express Genomics</b> , Co-founder & President & CEO  | New Enterprise Associates, General Partner (beginning in 2001):<br><b>Glyco Mimetics</b> , Investor & director<br><b>Psyadon Pharmaceuticals</b> (FKA Ruxton Pharmaceuticals), Investor & director<br><b>Supernus</b> , Director<br><br>Former director:<br><b>CoGenesys</b> (spinoff of HGS, acq'd by Teva Biopharmaceuticals)<br><b>IOMAI</b> (acq'd by Intercell AG) |
| Joel Jesse, VP R&D   | <b>Molecular Transfer</b> , Founder, CEO & CSO  |   |
| Dan Komarek, Sr Mgr, Gene Discovery Services                         | <b>Molecular Transfer</b> , Pres & COO  |   |
| Javed Siddiqi, Sr. Scientist   | <b>DNA Technologies</b> , Founder   |   |
| Mark Smith, developer of cDNA synthesis & cloning technology         | <b>Express Genomics</b> , Co-founder & Vice President & CSO   |   |
| Eric Winzer, CFO   | <b>Avalon</b> , CFO<br><b>OpGen</b> , CFO<br><b>Invitrogen</b> , CFO  |   |
| Derek Woods, VP R&D  | <b>Atto Biosciences</b> (acq'd by BD) CEO<br>Director, <b>Molecular Transfer</b><br>Director, <b>Adlyfe</b>   |   |

**Genetic Therapy** alumni include Rachel King,<sup>4</sup> CEO, **Glycomimetics**; Michael Kaleko, Sheila Connelly, and Tianci Luo, co-founders, **Advanced Vision Therapies** (acq'd by Gaithersburg-based S. Wohlstadter's **BioVeris** 2006, which in turn was acq'd by Roche in 2007); Michael D. Casey, Pres. & CEO, **Matrix Pharmaceuticals** (acq'd by Chiron 2002); Margot Mongold, Director of Human Resources at GTI, also filled senior HR roles at **Entremed**, **GenVec**, and is now consulting with **GlycoMimetics** and others on human resources; and Yung-Nien Chang, CSO, **PapiVax**.

<sup>3</sup> GlobalStem is the commercial research products and services component of Molecular Transfer, Inc.

<sup>4</sup> Current BIO Board President, former Entrepreneur-in-Residence NEA.



Medimmune was founded as Molecular Vaccines, Inc. by Wayne T. Hockmeyer in 1988, then in 1989 incorporated and changed its name to MedImmune, Inc. In 2007 AstraZeneca acquired MedImmune for \$15.2 billion, primarily for the assets in MedImmune's drug development pipeline. AstraZeneca then merged MedImmune with Cambridge Antibody Technology (acquired in 2006) to form a biologics division. MedImmune has a strong vaccine business, including its H1N1 and seasonal FluMist vaccines.

**Table 3. MedImmune**

| <b>MedImmune Employees:</b> Position held at MedImmune  | <b>MedImmune Employees:</b> Subsequent jobs  |
|---|--|
| Joseph Amprey & Peter Kiener  | <i>Zyngenia</i> Co-founders; CBO and CEO (2011)  |
| James Bingham, Research Associate   | <i>Human Genome Sciences</i> , Research Associate (1989-90)  |
| Luis Branco, Research scientist   | <i>Human Genome Sciences</i><br><i>Zalgen</i> , Founder  |
| Mel Booth, COO (from HGS)   | <i>Genstar Capital</i> , Advisor   |
| Edward Connor, CMO  | <i>ReveraGen BioPharma</i> , Interim CEO (2011)  |
| Frank Cworka, Jr., VP of Sales  | <i>Osiris Therapeutics</i> , Vice President and General Manager of Wound Care  |
| Peter Greenleaf, President  | <i>Sucampo Pharmaceuticals</i> , CEO<br>Histogenics (MASS), CEO (2013)   |
| <b>Wayne Hockmeyer, Co-founder; President and CEO (from Walter Reed Army Institute of Research)</b> | Baxter International, Director<br><i>Genvec</i> , Director   |
| Scott Koenig, SVP Research  | <i>MacroGenics</i> , President and CEO   |
| David Mott, President and CEO   | <i>New Enterprise Associates</i> , Partner, head of health care venture practice (2008)<br><i>Zyngenia</i> , COB         |
| Eric Richman  | <i>Pharmathene</i> , CEO   |
| Michael Richman, SVP Corporate Development  | <i>Genvec</i> , Board member; <i>Amplimmune</i> , CEO (until acquired by MedImmune in 2013; <i>MacroGenics</i> EVP & COO |
| Frank Top, CMO (formerly Walter Reed Army Institute of Research)                                    | <i>GlycoMimetics</i> , current Board member  |
| James Young, R&D Chief  | 3-V Biosciences (CALIF), Board member (2010)   |

In November, 2014, AstraZeneca announced plans to expand its biologics manufacturing center in Frederick, Maryland. The \$200-million-plus project will, expected to be completed in mid-2017, will add approximately 40,000 sq. ft. of manufacturing, laboratory and administrative space and bring a total of 300 new jobs to the site. Also in November of 2014, MedImmune agreed to acquire Definiens, a privately-held company that has pioneered a world-leading imaging and data analysis technology, known as Tissue Phenomics™, which dramatically improves the identification of biomarkers in tumor tissue. Earlier in 2014, MedImmune announced an expansion of its bioresearch collaboration with the University of System of Maryland (USM). The partnership with the University of Maryland Baltimore started in 2013 and expanded to campuses in College Park and Baltimore County. Research will start on five projects under the expanded agreement, which calls for five year commitments of at least \$5 million by MedImmune, \$800,000 the first year by the USM institutions, and \$200,000 the first year by the Maryland Department of Business and Economic Development.



Human Genome Sciences (HGS) was founded in 1992 by William A. Haseltine, a Harvard professor and AIDS researcher. HGS notable accomplishments are its approval of Benlysta (lupus), and a lucrative government contract for developing Abthrax (raxibacumab) for anthrax disease. HGS has award winning facilities at its Rockville, Maryland campus. In 2012, GlaxoSmithKline (GSK) was acquired by GlaxoSmithKline (GSK) for \$3.6 billion.

**Table 4. Human Genome Sciences**

| <b>Employees: Position held at HGS</b>                 | <b>Human Genome Sciences Employees: Subsequent jobs</b>   |
|--|---|
| M. James Barrett, Director, CoGenesys (spinout of HGS) | See <b>Life Technologies</b> , Table 1  |
| James Bingham, Scientist                               | <b>Lonza</b> , Assoc Dir Microbial R&D<br><b>Amplimmune</b> , VP Development & Marketing  |
| Mel Booth, Chairman & President                        | <b>MedImmune</b> , Chair & President<br>Advisor, <b>GenStar Capital</b>   |
| Luis Branco, Leader, Stable Cell Development Group     | <b>Zalgen Labs</b> , Founder and CEO  |
| Alain Cappeluti, VP Financial Operations               | <b>CoGenesys</b> ,<br><b>NexImmune</b> , CFO<br><b>ConverGene</b> , Managing Director<br><b>Noble Life Sciences</b> , President<br><b>BetaCat</b> , <b>ConverGene LLC</b> , <b>NexImmune</b> investor   |
| Kenneth Carter, Senior Scientist                       | <b>Avalon Pharmaceuticals</b> , Co-Founder<br><b>NeoDiagnostix</b> , Co-founder, CEO, Director<br><b>NexImmune</b> , CEO<br><b>Noble Life Sciences</b> , Co-founder, CEO, Director  |
| Linda Chang, Senior Director of Finance                | <b>PharmAthene</b> , SVP & CFO  |
| Margaret Fleming, clinical oncology professional       | <b>Amplimmune</b> , Senior Director, Clinical Operations<br><b>MacroGenics</b><br>Previously: <b>MedImmune</b> , <b>GlaxoWellcom (now GSK)</b>  |
| Stephen Garvey, second employee                        | <b>Avalon Pharmaceuticals</b><br><b>Noble Life Sciences</b> , Co-founder  |
| <b>William Hazeltine</b> , Founder, CEO, COB           | <b>Leukosite</b> , Co-Founder<br><b>Profectus Biosciences</b> , Director  |
| Jeffrey M. Herbst, Director of Clinical Development    | <b>Gliknik</b> , Senior Director, Clinical Development<br><b>GeneSys</b> , Director, Clinical Development<br><b>Teva Global Innovative Research &amp; Development</b><br><b>Zyngenia</b> , Senior Director, Clinical Development  |
| Steven Hubert, Scientist                               | Previously: <b>Genetic Therapy</b> , <b>Omnia Biologics</b>   |
| Kevin McGraith, Vice President, Hepatology Franchise   | Previously: Genentech; <b>WellDoc</b> , President   |
| Henrik S. Olsen, founding employee                     | <b>Artesian Therapeutics</b> , Founder<br><b>Celera</b><br><b>Gliknik</b> , VP drug discovery   |
| Jerry Parrott, VP Corp Commun & Public Policy          | <b>BioMarker Strategies</b> , President, CEO & Director   |
| David Stump, Sr. VP, Drug Development                  | <b>MacroGenics</b> , Director   |
| Wei-Wu He, research associate                          | <b>CASI Pharmaceuticals</b> (formerly <b>EntreMed</b> ) Co-founder<br><b>Emerging Technology Partners</b> investment fund, Co-founder (with Bill Snider)<br><b>EntreMed</b> , Executive COB<br><b>OriGene</b> , Founder and President<br><b>Investor</b> through Emerging Technology Partners<br>(some have been acquired or no longer operational): <b>Aptus Pharmaceuticals</b> , <b>Atto Biosciences</b> , <b>Avalon Pharmaceuticals</b> , <b>EntreMed</b> , <b>FASgen</b> , <b>Informax</b> , <b>IOMAI</b> , <b>MacroGenics</b> , <b>Marligen Biosciences</b> , <b>Psychiatric Genomics</b> |

*Note to Table 3: A group of HGS alumni, most notably Ken Carter and Alain Cappeluti, has moved on to play complementary or sequential executive and/or investor roles in Avalon Pharmaceuticals, NexImmune, and Noble Life Sciences, where former HGS alumnus Stephen Garvey joined them along with former Avalon leaders Stephen Horrigan, Jeffrey Strovel, and Eric Winzer.*

At the same time that investor Alan Walton (Oxford Science Partners) helped establish HGS, he created a non-profit [The] Institute for Genomic Research (TIGR). TIGR has also spun off several companies. TIGR's co-principal Craig Venter, the former NIH gene sequencing pioneer, subsequently co-founded **Celera Genomics** in Rockville in 1998 (moved to California and acquired by Perkin Elmer) and, more recently, Human Longevity (California and Baltimore). Claire Fraser, the other Principal at TIGR, is now Professor of Medicine and director of the Institute for Genome Sciences at the University of Maryland Baltimore.

Like MedImmune's acquisition of AstraZeneca, GlaxoSmithKline's 2012 decision to acquire Human Genome Sciences has been followed by an announcement of a planned facility expansion. GSK has recently (March 2015) acquired Novartis' vaccine business and is ramping up its capacity. A new global vaccine research and development center in Rockville at HGS's former facility will consolidate GSK's vaccine research labs now in Massachusetts and Pennsylvania, employing approximately 1,000 workers. GSK's other global R&D centers are in Rixensart, Belgium and Siena, Italy.



### CASE STUDY: Amplimmune's bounty

From the start-up's point-of-view, **Amplimmune** provides an example of Maryland pillar companies' rich sources of research and executive talent for young companies. Based on technologies developed by its founder, Dr. Lieping Chin and Dr. Drew Pardoll (JHU), the company is developing novel therapeutics for cancer and autoimmune and infectious diseases through immune system modulation. Amplimmune was acquired by **Medimmune** in 2013.

FOUNDER: Lieping Chen, MD, PhD (China-born and trained, now at Yale and **JHU**) First to use costimulation to enhance tumor immunity in 1992

PRESIDENT & CEO: Michael Richman

*Previously:*

- Dir., Corporate Business Development, **Chiron** (now *Novartis*)
- SVP **Medimmune** (now *AstraZeneca*)
- EVP **MacroGenics**

SVP & COO: Gary Fanger

*Previously:*

- VP Business Devt, **MacroGenics**

SVP & CSO: Sol Langermann

*Previously:*

- Multiple scientific posts at **Medimmune**

VP DEVELOPMENT & MARKETING: James Bingham

*Previously:*

- Associate Director Microbial R&D, **Lonza**
- Manager, **HGS**
- Manager, **Medimmune**

SR DIRECTOR, CLINICAL OPERATIONS: Margaret Fleming

*Previously:*

- Glaxo Wellcom (now *GSK*)
- **Medimmune**
- **Human Genome Sciences**
- **MacroGenics**

## B. Human Capital Characteristics

The human capital characteristic that remains unchanged from 1.5 decades ago: federal labs and universities continue to be important sources of entrepreneurs and managers, both directly and after they have worked in industry for a period of time.

As the 2002 report noted, the result of growing liberalization of intellectual property and conflict of interest policies and support for entrepreneurship at universities makes it increasingly possible to maintain university positions while helping to launch or support new ventures. However, fewer than 10

percent of company founders in 2015 are university-based, and only a handful of the firms were launched by federal laboratory employees. In contrast, the 2002 study found that fewer than 50 percent of founders had worked in industry immediately before launching their companies.

### C. Young biohealth entrepreneurs are emerging while still college students

In response to student demand, universities are giving increased attention and resources to students' entrepreneurship classes, internships, and opportunities to start their own companies. The current inventory reveals an exciting mix of science, engineering, and business student-entrepreneurs. Examples excerpted from websites include:

- **Proscia** is a Johns Hopkins students' start-up aimed at producing digitized biopsy images that can be shared easily to bring more precise analysis to the variable interpretation by individual radiologists. In addition, the Johns Hopkins Center for Bioengineering Innovation and Design (CBID) has generated student teams that have formed six medical device start-up companies.
- **Quantified Care**, formerly known as the Smartphone Physical, was founded in 2013 by JHU graduate students in bio-engineering and medicine. Its aim is to help healthcare organizations manage gaps in patient care through a mobile engagement platform through which patients receive proactive, individualized feedback, education, and clinical support leading to long-term behavior change and self-management, which ultimately improves outcomes while cutting costs.
- **Rehabtics** was founded by a Chinese graduate student at the Johns Hopkins Department of BioEngineering. In response to her discovery of the lack of effective low-cost solutions for patients to conduct long-term guided physical rehabilitation at home, she launched Rehabtics. With support from an enviable set of experts she developed a prototype that is being tested in a number of medical centers. Using Rehabtics' technology, caregivers are able to prescribe rehab exercises online, monitor patients' progress and give feedback remotely. Patients are able to rehab by playing customized motion-controlled video games. Their performance – such as range of motions and compensation movements – is tracked and logged in real time, which can be reviewed further by their caregivers online. The system can give patients automatic feedback and correction when patients make compensation movements. For home-bound patients, caregivers are able to conduct video calls with patients remotely with Rehabtics built-in video conferencing functions. (See case study at the end of the report.)
- **Vitus Animal Health** is an initiative building on a team project completed by students at the University of Maryland Smith School of Business from 2012-2013. The company is a collaborative venture among people with very diverse backgrounds and expertise, and is now a growing company with one simple goal: to make it easier for veterinarians and pet owners to share information.
- **Remedium Technologies** was founded by Matthew Dowling while he was still a doctoral student at the University of Maryland's Fischell School of Bioengineering. The trauma medicine company has utilized a number of federal and Maryland programs, including the University of Maryland's Mtech Technology Advancement Program incubator and the MIPS program, as well

as federal Small Business Innovation Research grants in the development of its blood-clotting foam product, which has recently received FDA approval.

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## IV. Technology changes over the decade

Once again, the technologies being leveraged by Maryland's biohealth companies reflect continued advances and trends in the sector since the early 2000s.

### A. Convergence of biology, information, and engineering technologies

#### i. Medical devices

Convergence is seen most clearly in the emergence of ingenious new medical devices for varied purposes: Devices for surgery companies include **BioAccess** (orthopedics), **BlueTorch Medical Technologies** (navigating to avoid nerves), **Gryphon Technologies** (RFID instrument tracking), **Harpoon Medical** (repairing mitral valve on beating heart), **ImageGuide** (image-guided robot-assisted surgery systems), and **Perceptive Navigation** (integration of ultrasound guidance with needle access). New diagnostic devices include **GraftWorx** (detects blockages of peripheral arterial bypass grafts) and **Innervation** (capsule endoscopy system to detect small bowel disorders). Therapeutic devices include radiological **Breethe** (portable artificial lung), **Clear Guide Medical** (*can be used on any ultrasound device to guide the interventionalist to a lesion*). **InnoVital Systems** (universal device for performing cricothyrotomies in battlefield medicine and domestic situations). Engineered therapeutics producers include **CERCA Solutions** (photodynamic therapy), **eNeura** (magnetic stimulation for migraine), and **Labyrinth Devices** (inner ear implants.)

#### ii. Carbohydrate biology, or glycobiology

Enhanced understanding of the role carbohydrates play in important biological processes has been made possible by technology innovations in mass spectrometry, sensitive array detector technology, and advanced software programs. Used in combination, they are permitting the discovery and synthesis of new classes of drugs known as glycans – polysaccharides, or sugar chains and glycomimetic compounds (small molecule mimics of functional carbohydrates). Glycobiology-derived drugs already on the market such as heparin demonstrate the great promise of these molecules, which are being explored as treatments for cancer.

**GlycoMimetics**, co-founded by Rachel King, uses novel and proprietary glycobiology technology developed by its co-founder John Magnani to formulate treatments for diseases, with an early focus on sickle cell disease, acute myeloid leukemia, and cancers. **Glycomantra**, a 2015 Maryland Innovation Initiative award winner, is developing carbohydrate-based therapies for cancer and infectious diseases, **Glycotex** is a clinical stage biopharmaceutical company focused on discovering and developing a novel class of drugs intended to accelerate human wound healing and tissue repair (see Chapter IV, Returning Veterans) in acute and chronic wounds. **Glygen** offers various solid phase extraction devices for sample purification for mass spectrometry. **Kamtek's** research products include custom microarray printing including glycan arrays. **Trophogen** is developing high affinity glycoprotein hormone and related growth



factor analogs for human and animal infertility as well as targeted therapy and imaging of thyroid, ovarian, breast, prostate and testicular cancers.

## **B. Progress toward personalized / precision medicine**

Dramatic reductions in the cost of sequencing human genomes and other molecular analysis have propelled the maturation of personalized medicine to precision medicine. Protein and molecular biomarkers — hormone, receptor, and protein assays — are being used for diagnosis, therapy selection, therapy monitoring, and early detection of recurrence, particularly of cancer.<sup>5</sup> Maryland companies are using bioinformatics analysis, including “big data” processes; advances in imaging and digital analysis; improved hormone, receptor, and protein assays, including multiplexed and miniaturized tests that maximize use of tissue samples; non-invasive techniques; next generation sequencing, mass spectrometry and PCR; molecular and nanoscale diagnostics, and emerging capabilities for detecting circulating DNA and RNA molecules and their methylation patterns.

### ***i. Tools: Molecular diagnosis***

Firms in Maryland include: Adera, Akonni Biosystems, Alper Biotech, DioGenix, and Media Cybernetics (imaging), and TrimGen.

### ***ii. Tools: Bio-nanotechnology***

Firms include: Allegiance NanoSolutions, Aparna, AsclepiX, and Avanti Nano.

### ***iii. Tools: Big data***

The BIG DATA analytics firm, *Insilico Medicine*, is focused on using analytics for drug discovery and personalized medicine for aging and age-related disease.

### ***iv. Immunotherapy***

The *MIT Technology Review* calls immunotherapy the most important medical breakthrough of the year.<sup>6</sup> Mobilizing a body’s own immune responses to disease requires exquisitely personalized medicine. Maryland companies active in this area include: **Amplimmune** (therapeutics for cancer and autoimmune and infectious diseases), **Avanti Therapeutics** (cancer, cardiovascular and other difficult-to-treat diseases), **Celimmune** (immunotherapy for celiac disease), **Champions Oncology** (cancer), **Insilico Medicine** (big data drug discovery and personalized medicine for aging and age-related disease), **Intrexon** (synthetic biology’s biomimetics applied to the challenges of immunology), **MacroGenics** (therapeutics for cancer, autoimmune disorders and infectious diseases), **Magnifygen** (immune-biomarker for cancer), **NexImmune** (immunotherapy), **Northwest Biotherapeutics**<sup>7</sup> (personalized

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<sup>5</sup> Kalorama Diagnostic Analyst (2014), “The World Market for Cancer Diagnostics, 5<sup>th</sup> Edition: Precision and Personalized Testing Arrives,” PRNewswire, <http://www.prnewswire.com/news-releases/the-world-market-for-cancer-diagnostics-5th-edition-precision-and-personalized-testing-arrives-258035251.html>.

<sup>6</sup> Antonio Regalado, *MIT Technology Review*, “2014 in Biomedicine: Rewriting DNA, Decoding the Brain, and a GMO Paradox,” December 20, 2014.

<sup>7</sup> Founded in 1998; April 2015 Woodford Investment Management LLP invested an additional \$40 million (after \$25M in November 2014) in the company.

immune therapies for solid tumor cancers), **PepVax** (immunotherapies for cancer), and **Vaccinogen** (producer of OncoVAX<sup>®</sup>, the only immunotherapy for Stage II colon cancer).

#### ***v. Inflammatory and autoimmune diseases and cancer***

Inflammation, one of the body's innate immunity responses, can lead to a host of diseases, such as hay fever, periodontitis, atherosclerosis, rheumatoid arthritis, and even cancer (e.g., gallbladder carcinoma). Inflammation is therefore normally closely regulated by the body. The large variety of proteins involved in inflammation are vulnerable to genetic mutation that impairs or otherwise dysregulates the normal function and expression of individual proteins. Disorders associated with inflammation include: acne vulgaris, asthma, autoimmune diseases, autoinflammatory diseases, celiac disease, chronic prostatitis, glomerulonephritis, hypersensitivities, inflammatory bowel diseases, pelvic inflammatory disease, reperfusion injury, rheumatoid arthritis, sarcoidosis, transplant rejection, vasculitis, and interstitial cystitis. In Maryland, **CASI Pharmaceuticals** (formerly EntreMed), **Cureveda** (respiratory diseases), **Cynca Laboratories**, **Gliknik** (autoimmune diseases and cancer), **Leukosight**, **MacroGenics**<sup>8</sup>, **Medigen**, **M.J. Burg**, **NourImmune**, **Osiris**, and **Sucampo**, **Wellstat Immunotherapeutics** are developing diagnostics and therapeutics to address the intertwined challenges of inflammatory and autoimmune disease.

Two young Maryland companies bring new technologies and approaches to these persistent challenges. In February, 2015, **Celimmune LLC**, a newly-created clinical development-stage immunotherapy company targeting autoimmunity and inflammation, announced that it will initially focus its distinctive core competence in translational medicine, immunotherapy clinical development and commercialization on combating celiac disease. **Benevir Biopharm** (a BHI company), founded in 2011, licensed exclusively from NYU an improved therapeutics platform based on oncolytic virotherapy for the treatment of a wide variety of solid tumor cancers. Oncolytic viruses operate through two mechanisms: (1) direct killing of cancer cells through tumor-specific viral replication, and (2) induction of an anti-tumor immune response that eliminates metastases. Until recently, this promising technology had been hampered by immune system recognition and clearance by the body. The Benevir platform, BV-2711, hides from the immune system, maximizing the virus' spread through a tumor. BeneVir has received two Phase I SBIR awards to develop this promising technology for the initial indications of bladder cancer and glioblastoma. In 2014, the company closed a Series A investment round of \$12M with Pansend, LLC, an indirect wholly-owned subsidiary of HC2 Holdings, Inc.

#### ***vi. Biomarkers and targeted therapies for cancer***

These are being developed by **BioMarker Strategies**, **BioSciCon**, **Cellona Therapeutics** (melanoma), and **CellPath Therapeutics** (personalized chemotherapy). The new wave of cancer therapeutics includes: **Alper Biotech** (diagnostics to identify cancer proteins in tissue and blood), **ConverGene** (MYC-targeted therapeutics), **MacroGenics** (monoclonal antibody-based), Medigen (vaccines), **OncoPlexDX**, and **PapiVax** (cervical cancer). (See III.C.2 Therapeutic Vaccines.)

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<sup>8</sup> Began Phase I study March 2015 – triggering a \$3M milestone payment from Takeda – of a bi-specific molecule that targets two B-cell proteins for treatment of autoimmune disorders.

### ***vii. Other novel cancer treatments***

**BetaCat Pharmaceuticals** is developing small molecule inhibitors of beta catenin which stop the oncogenic activity of WNT pathway signalling without causing toxicity to normal tissue, initially focused on colorectal cancer, myelodysplastic syndromes (and AML), and multiple myeloma; **Cellona Therapeutics** (RAS signaling pathways and family of onco-proteins in cancer cells, with a focus on melanoma); **CERCA Solutions** (Photodynamic Therapy *PDT* for diagnosing and treating cervical cancer, already being used to treat esophageal, colon, and skin cancers); **Chikujee Therapeutics** (use of proprietary multi-functional nanoparticles in NanoBindi architecture make it possible to engineer complex drug molecules to advance personalized medicine); **GlycoMimetics** (compounds targeting the tumor microenvironment to enhance the efficacy of chemotherapy, with initial applications in blood cancers such as AML and myeloma); **MacroGenics** (next-generation antibody technology platforms with product candidates that target several solid tumor types as well as hematological malignancies); **Magnifygen** (“immunogenicity-abolished anti-ROR1 immunotoxin” technology for treatment of various kinds of cancer, especially triple-negative breast cancer or TNBC), **Rexahn Pharmaceuticals** (three targeted cancer treatment candidates for melanoma, cancers of the ovary, kidney and pancreas; solid tumors in the pancreas, lung, colon, kidney and others; and metastatic renal cell carcinoma, respectively); **Shuttle Pharmaceuticals** (using technology based on epigenetic regulation of gene expression that leads to changes in cellular radiation responses, is developing products with unique properties to sensitize cancer cells, protect normal tissues, and monitor clinical response to treatment; technology was licensed from Georgetown University); **TDP Biotherapeutics** (licensed technology for a highly targeted anticancer drug that interferes with a protein manifested by cancer cells but not by normal cells); **Wellstat Biologics** (pipeline of oncolytic viruses in development); and **Zylacta** (antifibrotic therapy capable of halting, and even reversing the progression of liver fibrosis to cirrhosis and cancer).

### ***viii. Convergence of personalized therapeutics and diagnostic medical devices***

“Companion diagnostics” are devices – usually *in vitro* or imaging – used to monitor how effectively and safely a therapeutic product is working for a specific patient. The monitoring helps identify which patients might benefit most from the therapeutic and those for whom there are increased risk of serious side effects. It also helps clinicians to adjust treatment to achieve better safety or effectiveness. The U.S. Food and Drug Administration (FDA) issued guidance on *in vitro* companion devices last summer and has approved/cleared several specific devices developed by **Qiagen** and **Life Technologies**. **Ariadne Diagnostics** is also developing companion diagnostic tests in areas of oncology and rare neuromuscular/neurodegenerative diseases.

## **C. Acquired immunity: Maryland has the top vaccine cluster in the country**

The founder of MedImmune, the pillar company in this sector, Wayne Hockmeyer, was chair of the department of immunology at Walter Reed Army Institute of Research when venture capitalist Wallace

Steinberg (Health Care Ventures) provided \$3.5 million to start the company. Today, not only are new vaccines being developed, but also new uses for vaccines have emerged.

### ***i. Prophylactic vaccines***

Companies in Maryland include: **Aeras** (a nonprofit focused on tuberculosis), **Astra Zeneca** (acquirer of MedImmune whose Synagis vaccine<sup>9</sup> prevents a respiratory infection that can be fatal to premature and sickly infants), **Emergent BioSolutions**, which acquired DynPort and other companies with manufacturing capabilities (anthrax, tuberculosis booster vaccine), **GenVec** (infectious diseases including respiratory syncytial virus, herpes simplex virus, dengue fever, influenza, malaria), **GlaxoSmithKline** (establishing a new vaccine center in Montgomery County), **ImQuest Biosciences** (anti-infectives), **Integrated BioTherapeutics** (anti-infectives), **Lentigen** (prevention of HIV/AIDS, pandemic influenza), **Longhorn Vaccines and Diagnostics** (influenza and tuberculosis), **Medigen** (infectious disease), **Novavax** (influenza, Respiratory Syncytial Virus), **Pearl Life Science Partners** (infectious enveloped viruses), **PharmAthene** (bioterrorism agents such as anthrax), **Plantvax** (inhaler to deliver butyrylcholinesterase, a biological scavenger of toxic substances such as nerve agents, insecticides, succinyl choline, and cocaine and an edible HIV vaccine), **Sanaria Inc.** (malaria), **TenGen Biomedical** (cervical cancer), **Vaxin** (influenza – nasal, anthrax), **Wellstat Vaccines** (candida, group A streptococcus, meningococcus).

### ***ii. Vaccines for therapeutic uses***

Maryland companies include: **AnGes** (human papillomavirus), **AriaVax** (helicobacter pylori, RSV and HIV-1), **BioMimetics** (AIDS, respiratory agents, influenza virus, rhinovirus, non-typeable haemophilus influenza, malaria and dengue), **Emergent BioSolutions** (chronic lymphocytic leukemia), **Immunomic Therapeutics** (allergies), **Medigen** (cancer), **PapiVax** (high-grade precancerous cervical lesions), **Precision Biologics** (cancer vaccines), **Profectus BioSciences** (treatment and prevention of infectious disease and related cancers), **SynAm Vaccines** (pneumococcal diseases), and **TenGen Biomedical** (HPV, West Nile Virus and coronavirus),

### ***iii. Vaccine development and manufacturing contractors***

Maryland firms include **Amarex Clinical Research**, **APC Biotechnology Services**, **AVANZA Laboratories**, **Axella LLC**, **BIOQUAL, Inc.** (FKA Diagon Corp), **BioStat Solutions**, **Fina BioSolutions LLC**, **Innovative Biotech Inc.**, **MaxCyte**, **Omnia Biologics**, **Paragon Bioservices, Inc.**, **ProSpect Pharma, Inc.**, **SD Nanosciences** (MedImmune contract to explore possible use of bubble delivery technology for vaccines), and **Washington Biotechnology, Inc.**

### ***iv. University vaccine development resources***

**The University of Maryland School of Medicine's Center for Vaccine Development (CVD)**, established in 1974, has earned an international reputation as an academic vaccine development enterprise for creating and testing vaccines against cholera, typhoid fever, paratyphoid fever, non-typhoidal Salmonella disease, shigellosis (bacillary dysentery), Escherichia coli diarrhea, malaria, and other infectious diseases, including influenza. In addition to its research and outpatient facilities in Baltimore, Maryland, the CVD has fixed facilities to conduct clinical studies in Mali, West Africa, Malawi, Southern

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<sup>9</sup> Early support for this product's development was provided by the University of Maryland's MIPS program.

Africa and Santiago, Chile and can undertake time-limited field studies in many other countries in Africa, Asia and Latin America.

**The Johns Hopkins Center for Immunization Research (CIR)** is a leader in vaccine evaluation and Good Clinical Practice (GCP) training. Established at what is now the Bloomberg School of Public Health in 1985 by Dr. Mary Lou Clements-Mann, the CIR is one of the nation's leading vaccine research centers.

#### ***v. Federal laboratories and agencies***

However, the key elements of the funding, research, and talent infrastructure for vaccine development in Maryland are the federal laboratories: Walter Reed Army Institute of Research, U.S. Army Medical Research Institute for Infectious Diseases and the National Cancer Institute at Fort Detrick, Walter Reed National Military Medical Center, the National Institute of Allergy and Infectious Diseases (NIAID), the Centers for Medicare and Medicaid, and the Food and Drug Administration. For example, the Division of AIDS (DAIDS) was formed in 1986 at the National Institutes of Health's NIAID to develop and implement the national research agenda to address the HIV/AIDS epidemic. Federal funding for HIV/AIDS research, prevention, and treatment has grown from \$200,000 in FFY1981 to \$30B in 2015. One half of Maryland's vaccine companies were founded since 2000. See Section IV.B.

#### ***vi. Infectious diseases***

Maryland companies developing or supporting the development of non-vaccine therapeutics for infectious diseases include: **Advanced Biotechnologies** (virology products for therapeutics developers), **BD Diagnostic Systems**, **Biaera Technologies** (builds and sustains aerobiology programs, equipment, training, and resources to enable its customers to conduct infectious disease research), **Bio-Factura** (biodefense), BioWorld Consulting Laboratories (fully human monoclonal antibodies and diagnostic assays for infectious diseases), **Functional Genetics** (influenza), **GenVec** (RSV, herpes simplex, dengue fever, influenza, malaria), **GlycoMantra** (carbohydrate-based therapies for cancer and infectious diseases), **IATRICa**, Inc., (novel targeted immunoconjugates), **ImQuest Biosciences** (CRO that rapidly identifies therapeutic agents with the potential to inhibit the replication of infectious agents), **Integrated BioTherapeutics** (staph and filovirus family, which includes ebola and Marburg viruses), **Lupin Pharmaceuticals** (Suprax® anti-infective product in pediatric and other physician practices), **MacroGenics** (targeted immunotherapies), **MycoMed Technologies** (diagnostics and therapeutics for fungal infections), **MyGenostics** (device for detection of aspergillus), **N&N Scientific** (antiviral), **Novavax**, **PathSensors** (develops environmental tests for infectious disease pathogens), **PharmAthene**, **Scanogen** (easy inexpensive access to info present in patient samples for 1. point-of-care detection of infectious diseases), **Safe Equine Technologies** (diagnostics for infectious diseases), **Sequella** (novel antibiotics for global infectious disease, including pulmonary tuberculosis and helicobacter pylori), **SYSTAAQ Diagnostic Products** (developing real-time PCR based assays and molecular diagnostic test solutions for infectious disease), **Tetracore** (diagnostic reagents and assays for infectious diseases and biological warfare threat agents), **Virusys** (manufacturer of infectious disease antigens and antibodies), and **Z-BioMed Inc.** (influenza and tuberculosis).



### **CASE STUDY: MacroGenics**

**MacroGenics**, founded by a former MedImmune SVP for Research in 2000, illustrates the continuing role the federal government has played in the launch and success of this company. Unlike many new firms, it began with a platform technology (Fc Optimization, which enhances the natural immune system's ability to mediate killing of cancer cells and attenuate autoimmune disorders) and a private investment stake, and continues to blend public and private funding. MacroGenics has attracted significant outside investment from multiple pharmaceutical and biotechnology collaboration partners, generating hundreds of millions of dollars of capital for the Company to further advance its pipeline. In addition, the company has raised in excess of \$450 million in venture capital and public equity from investors over the past 15 years, as illustrated in Table 5 on the following page.

**Table 5. MacroGenics Grants, Contracts, and Investments from its Founding in 2000**

| Grants & Govt Contracts |        |                     |              | Grant project name/Description of private funding   | Private investment   |
|-------------------------|--------|---------------------|--------------|---|----------------------|
| Year                    | Agency | Type                | Amount Spent |   |                      |
|                         |        |                     |              | <i>Market cap: 8/19/15 ~\$1.0B (NASDAQ)</i>   |                      |
| <b>2014-2015</b>        |        |                     |              | Follow-on equity offerings  | ~\$260,000,000       |
| <b>2013</b>             |        |                     |              | <b>IPO October 2013</b>   | <b>~\$74,000,000</b> |
| <b>2010-2015</b>        |        |                     |              | Capital generated from <u>nine</u> collaborations entered into between 2010-2015 (Janssen, Takeda (x2), Gilead, Servier (x2), Pfizer, Boehringer Ingelheim, Green Cross)  | ~\$300,000,000       |
| <b>2010</b>             | HHS    | Research Grants (3) | \$7,332,307  | Grants included: (1) preclinical IND-enabling activities related to Inflammation DART; (2) pan-Dengue virus immunotherapeutic for prevention and treatment, and (3) antibody-based therapy of Chikungunya virus   |                      |
| <b>2008</b>             |        |                     |              | Series D-2 financing (multiple tranches)  | \$46,000,000         |
| <b>2008</b>             |        |                     |              | Equity issued to acquire Raven Biotechnologies (cancer stem-like cell platform co. in South San Francisco)  | \$9,420,385          |
| <b>2007</b>             |        |                     |              | Collaboration with Eli Lilly re: teplizumab (anti-CD3 antibody for treatment of Type 1 Diabetes) (upfront + subsequent milestone payments)  | \$96,000,000         |
| <b>2007</b>             |        |                     |              | Juvenile Diabetes Research Foundation grant for global Phase 2/3 trial of teplizumab  | \$50,000             |
| <b>2006</b>             | HHS    | Research Grant      | \$2,653,563  | Monoclonal antibody therapy for West Nile Virus   |                      |
| <b>2006</b>             | HHS    | Research Grant      | \$6,135,344  | Cocktail of neutralizing mAbs for smallpox prevention   |                      |
| <b>2006</b>             | HHS    | R&D Contract        | \$32,921,642 | Development of therapeutic agents for West Nile Virus (NIAID)   |                      |
| <b>2006</b>             |        |                     |              | Series C financing  | \$45,000,000         |
| <b>2004</b>             |        |                     |              | Series B financing  | \$30,500,000         |
| <b>2004</b>             | HHS    | SBIR 1 (6 Awards)   | \$310,137    | Awards included: (1) melanoma proteins in serum and urine, (2) FcRIII blockade as treatment for autoimmune disease, (3) development of soluble FcR-Ig fusion proteins, (4) Role of anti-Fc Gamma RIIB antibody in tumor clearance, (5) development of novel Brucella vaccine candidates and (6) enhancement of immune response by Fc modification |                      |
| <b>2003</b>             | HHS    | SBIR 1+2 (5 Awards) | \$1,307,662  | Awards included: (1) superantigens in EBV pathology, (2) plasma membrane proteins in prostate cancer, (3) cutaneous T-cell lymphomas, (4) vaccine discovery for Burkholderia via protection screen, and (5) enhancement of immune response by Fc modification   |                      |
| <b>2003</b>             |        |                     |              | Genzyme strategic partnership & equity investment   | \$5,000,000          |
| <b>2002</b>             | HHS    | SBIR 1              | \$100,000    | Enhancement of immune response by Fc modification   |                      |
| <b>2002</b>             |        |                     |              | Acquired Eliance, formed immunotherapeutics partnership with UT Southwestern  | \$12,600,000         |
| <b>2001</b>             |        |                     |              | Second tranche of Series A financing; hiring of Dr. Scott Koenig  | \$13,500,000         |
| <b>2000</b>             |        |                     |              | August: Incorporation by scientific founders Drs. LeRoy Hood, Ruedi Aebersold, and Alan Aderem (Institute for Systems Biology, a nonprofit biomedical research organization based in Seattle), Jeffery Ravetch (Rockefeller University) and Scott Koenig (MedImmune)  | \$3,714,000          |

SOURCE: MacroGenics

## D. The brain: the now just-visible frontier

Neuroscience has benefitted enormously from new analytical tools and technologies, beginning with functional MRIs in the early 1990s. President Obama's signature science project is the U.S. BRAIN Initiative, a public-private research effort that aims to revolutionize our understanding of the human mind and uncover new ways to treat, prevent, and cure brain disorders like Alzheimer's, schizophrenia, autism, epilepsy, and traumatic brain injury. Maryland's companies represent the wide range of foci and approaches currently underway, many of them targeted on the Boomer Generation epidemic – Alzheimer's disease – which, after a generation of research, has failed to reveal a sure cause or recipe for preventing or treating it. Growing concern about concussive injuries to the brain has added to the urgency of brain science.

The Maryland companies include: **Adlyfe** (diagnosis of neurogenerative disorders), **AgeneBio** (therapeutics to delay Alzheimers), **Brain Biosciences** (diagnosis through molecular brain imaging), **Brain Sentry** (helmet-mounted concussion sensors), **BrainScope** (handheld tool to measure brain function at point-of-care), **CBH** (R&D services related to CNS disorders and rehabilitative care), **Cerecor** (pharmaceuticals active in the CNS), **DioGenix** (molecular diagnostics for neurological diseases such as MS and other immune disorders), **Gabriel Sciences** (advancing treatment and understanding of mental illness, with a focus on antidepressants), **L&J Biosciences** (neurogenerative), **Myotherapeutics** (neuromuscular diseases), **NeuralStem** (stem cells for CNS), **Neuren** (brain injury and degeneration), **Neuronascent** (therapeutics for neurogenerative diseases such as Alzheimer's and Parkinsons, and for depression), **OccuLearn** (visual cognitive screening and therapy), **Panacea Pharmaceuticals** (CNS), **Psyadon Pharmaceuticals** (serious psychiatric and neurological disease), **Psychnostics** (blood test diagnosis), **RemeGenix** (prevent and treat Alzheimer's disease), and **ReveraGen BioPharma** (neuromuscular disease).

## E. Aging and related maladies

Alzheimer's is but one of the disorders of an aging population that are receiving outsized attention now that the first inklings of the possibility of turning back the clock, or at least stopping it, have emerged. More than 70% of people over 65 have two or more chronic conditions like arthritis, diabetes, cancer, heart disease, and stroke.<sup>10</sup> In addition to the neuroscience-targeted firms listed above, Maryland companies focused on aging include: **AsclepiX** (macular degeneration), **Audiodontics** (teeth auditory device), **Genetik Signal** (core market is anti-aging products), **GenVec** (hearing loss and balance disorders), **Insilico Medicine** (big data drug discovery and personalized medicine for aging and age-related disease), **Irazu BioDiscovery** (delaying pathologies associated with aging), and **LKC Technologies** (visual electrophysiology).

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<sup>10</sup> Hung, Ross, Bookvar, and Siu, BMC Geriatrics 11:47 (2001), cited in "Medical Research: Treat Ageing [sic]," *Nature News & Comment* July 23, 2014.



## F. Diabetes and other metabolic disorders

As Americans grow heavier and heavier, obesity has led to a cascade of disorders, most notably diabetes, an autoimmune disorder. In cases of type 1 diabetes, the immune system attacks and destroys the specialized cells in the pancreas that produce insulin. When the body can no longer produce sufficient insulin (a protein that regulates blood glucose concentration) the resulting chronically high glucose levels in the blood (hyperglycemia) cause blood vessel and nerve damage. Complications/co-morbid conditions associated with diabetes include hypoglycemia, hypertension, dyslipidemia (high levels of LDL cholesterol), cardiovascular death and heart attack rates, stroke, blindness and eye problems, kidney disease, and amputations. In 2012, 29.1 million Americans, or 9.3% of the population, had diabetes, the 7<sup>th</sup> ranking cause of death. In 2012, diabetes costs – health care and lost productivity – totaled \$245 billion, and, after adjusting for population age and sex differences, average medical expenditures among people with diagnosed diabetes were 2.3 times higher than what expenditures would be in the absence of diabetes.<sup>11</sup> (See Chapter IV, Regulatory changes.)

Maryland companies addressing diabetes and/or obesity include **EDT OriGene Technologies**, a research tool company, which, in February of 2014, acquired BioCheck (CA), which produces in vitro diagnostics (IVDs) for diabetes. In March 2015, **MedImmune** announced a three-year collaboration with the Harvard Medical School's affiliate Joslin Diabetes Center, the world's preeminent diabetes research institution, to work together on new drug candidates that could someday regenerate insulin cells, increase calorie-burning "brown fat" or even replicate the effects of bariatric surgery. Joslin also has a location in Maryland at Doctors Community Hospital in Lanham. Additional active Maryland companies include **Senseonics** (Continuous Glucose Monitoring System, an implantable continuous glucose monitor), **Seraxis** (developing a cell therapy to treat insulin dependent diabetes), **Spherix** (long-time – founded in 1967 – innovator in biotechnology for therapy in diabetes, metabolic syndrome and atherosclerosis), **Vasoptic Medical, Inc.** (VMI) (early stage medical device company developing a retinal imager for early detection of diabetic retinopathy, a vision-threatening complication of diabetes), and **Washington Biotechnology** (CRO that provides full-service testing and research of in vivo studies including In vivo disease models of diabetes. In November 2014, Baltimore's **WellDoc** (mobile health technology to help manage type 2 diabetes) and Samsung announced a collaboration to improve the lives of people living with diabetes.

Other Maryland companies innovating in improving outcomes and reducing costs (see Chapter IV, Regulatory) of this chronic disease include **Telcare**, which has produced FDA-approved, HIPAA-compliant cellular-enabled wireless glucose meter. The company raised a \$32.5M Series C round in October 2014 from Norwest Venture Partners, Sequoia Capital, Qualcom Ventures and Mosaic Health Solutions. **Advanced Biometric Sensors** is developing a revolutionary hand-held glucose meter with innovative characteristics and patient benefits. The Little Deer device can measure glucose in a variety of specimens, including whole blood, serum or a venous blood specimen.

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<sup>11</sup> American Diabetes Association (2014). *National Diabetes Statistics Report, 2014*

In addition to diabetes, metabolic disorders span a broad swath of specific conditions manifested in most of the systems of the human body, including neurological disorders and stroke (acid lipase disease, Barth Syndrome, Central Pontine myelinolysis, Farbers Disease, gangliosidoses, Lesch-Nyhan Syndrome, lipid storage diseases, mucopolipidoses, mucopolysaccharidoses), muscle (mitochondrial myopathies, muscular dystrophy, skeletal (Hurler Syndrome), liver (Type I Glycogen Storage Disease, Type II GSD also called Pompe disease), kidneys (hyperoxaluria), and a number of rare genetic disorders, including Hunter Syndrome and [Trimethylaminuria](#).

## **G. Additional therapeutic foci**

*Asklepion Pharmaceuticals, HPM Diagnostics, Telcare, and Tengen Biomedical* have focused efforts to address liver-based disease. *Cytheris Inc.* (lymphopenia-driven), *ETX Pharma* (gastrointestinal diseases), *Ocular Proteomics* (eye diseases), *SAJE* (respiratory diseases) *United Therapeutics* (vascular disease such as pulmonary-arterial hypertension) and other Maryland companies are developing **therapies aimed at a wide variety of non-cancer targets.**

## **H. Delivery modalities for therapeutics**

Parallel to the development of new therapeutics, there have been advances in the ways in which they are delivered to their targets. *Alltranz* (dermal), *Axxia* (subcutaneous abuse-deterrent opiate drug delivery technologies for pain), *Bioactive Surgical* (surgical delivery systems for stem cells and bioactive molecules), *BioElectronics* (miniaturizing electromagnetic therapeutic applications into disposable, cost-effective dermal patches), *Capricorn Pharma* (oral), *GrayBug* (ophthalmic), *Intravenous Solutions*, *Kydes Pharmaceuticals* (topical microbicide for HIV prevention), *Medifocus* (hermotherapies), *MediSense Technologies* (shockwave therapy), *Meridian Medical Technologies* (auto-injector), *Otomagnetics* (delivery of therapeutics to inner and middle ear), *PharmaCyte Biotech* (live cell encapsulation technology), and *SD Nanosciences* (soap bubbles).

## **I. mHealth revolution – see “Regulatory” below, Section IV.**

## **J. University-based sources of technology.**

Universities in Maryland and around the country continue to provide sources of technologies for licensing as well as technical advising to Central Maryland entrepreneurs. Johns Hopkins University and the University of Maryland are particularly active in this endeavor.

Institutions like the University of Maryland continue to invest in endowed chairs placing the region at the forefront of recruiting and retaining talent. In April 2014, the Maryland General Assembly passed the E-Nnovation program where state government funding would match funds for the recruitment of endowed researchers across a set of disciplines that include medical and public health sciences, neurosciences.

### ***i. JHU Licensing***

*Animalgesics, AquaAnimal, AsclepiX, CardioSolv, Euveda, Gemstone Biotherapeutics,<sup>12</sup> HALO, MycoMed, Sonorax Surgical, and Vixiar Medical* and others have licensed start-up technology from Johns Hopkins University in the last 10 years.

### ***ii. USM Licensing***

*BioMedica, Breathe, GlycoMantra, Harpoon Medical, MedSense, Plasmonix, and SilcsBio* and others have licensed start-up technology from University System of Maryland component universities.

### ***iii. Other University Licensing***

Some Central Maryland entrepreneurs have also built their firms on technology discovered and/or developed at other schools around the country: *Benevir* (NYU), *GenetikSignal* (University of Washington), *Oncolmmune* (Ohio State University and University of Michigan), and *OpGen* (University of Wisconsin).



#### **MINI CASE STUDY: AsclepiX**

AsclepiX founded in 2014, illustrates several of the previously mentioned trends. The company employs technology licensed from Johns Hopkins University to tackle age-related macular degeneration. The company uses short biomimetic anti-angiogenic (anti-neovascular) and anti-lymphangiogenic peptides, and adds the latest biomaterials technologies and drug delivery modalities to produce long-lasting biodegradable nano- and microparticles that deliver biomimetic peptides throughout the body. In addition to ophthalmology, the approach has applications in oncology and other angiogenesis- and lymphangiogenesis-dependent diseases.

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<sup>12</sup> \$2.45 seed funding June 2015)

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## V. Contextual changes over the decade

The world within which biohealth entrepreneurs operate has changed significantly since 2002-2004, affecting both their challenges and their opportunities.

### A. Regulatory and payer requirements

Ten-to-fifteen years ago, health care providers were focused on meeting federal requirements associated with HIPAA and early transition to electronic health records (EHRs). Now, hospitals must demonstrate “meaningful use” of EHRs, and federal payers – Medicare and Medicaid, primarily – are in the ascendency. New products must not only be efficacious and safe for humans, but also demonstrate savings to payers compared to best in current use. The new “accountable health care” is the focus of Maryland companies *Allegiant*, *Live Healthier*, and *Quantified Care*.

Hospital concerns now must include not only medical error prevention, but also improvements in hospital efficiency without sacrificing medical effectiveness. Patient time in the hospital and readmits must be minimized to avoid jeopardizing Medicare/Medicaid reimbursements. The effective use of wireless technology combined with innovative medical devices and software tools can contribute; companies are responding to the opportunity. *Analytical Informatics*, *Avhana Health*, *Baton Health*, and *Get Real Health* have stepped up to the challenge of patient engagement. *Maven Medical's* software aims to produce better-informed medical decision-making.

Increasingly, the home is being perceived as a fourth locus for the delivery of health care, along with hospitals, clinics, and nursing homes as mobile health (mhealth) innovations proliferate. Maryland mhealth firms include: *Aegle* (“the Ark”), *Anthrotronix* (precise on-the-field measurement of concussive effect of head injuries), *Awarables* (sleep disorder diagnosis), *ClickMedix* (tele-connected community health workers serve as primary service deliverers), *emocha Mobile Health* (for remote patient app, multimedia platform for adherence, clinical trials and chronic diseases), *Flexible Medical Systems* (transdermal electrochemical sensor for remote medical diagnostics), *GetWell Network* (interactive patient care), *Mindoula Health*, *Vheda* (chronic disease management); *ArmAware* (hemiplegia), *Biocushion*, *BTE Laboratories*, and *Rehabtics* (rehabilitation and physical therapy).

*Arcion* is attacking the hospitalization minimization challenge on another front in response to medical practice that now attends closely to patients’ level of pain, which suppresses immune responses, hampering healing after surgery. Pain control promotes healing and mobility, and reduces hospital time. *Axxia Pharmaceuticals* produces a subcutaneous opiate delivery technology to deter abuse of this gold-standard chronic cancer-related pain remedy. *Bioelectronics Corporation* produces dermal thermal patches to allay pain. *Kydes Pharmaceuticals’* products in the pipeline include three for pain management and *Proove Biosciences’* testing improves the selection, evaluation and dosing of pain medicine.

## B. Heightened focus on personal and national security

Along with the push toward EHRs came concern about the privacy of patient records, which has been the purview of specialized large integrators such as EPIC, Cerner, MEDITECH, Allscripts, and units of I.B.M. that provide care and patient accounting systems and support for implementation within large health care systems. None of these firms is located in Maryland. However, **Protenus**, a new patient record security company, emerged last year from DreamIT Health's Baltimore accelerator (see V.D)

The ebola tragedy last year reminded everyone of the danger of pandemics, which had not been top-of-mind since the polio and smallpox epidemics in a far less mobile era. Ebola also awoke the fears of **bioterrorism** -- deliberately released deadly infective agents -- that had subsided as time from the 9/11 and anthrax and SARS attacks lengthened. Central Maryland companies that produce detection technologies and treatments include **Avanti Nanosciences** (endotoxins in biopharmaceuticals), **BioWarn** (biological substance detection and pathogen surveillance), **CosmosID®** (pathogen detection using software solutions that enable rapid metagenomics identification of biothreats), **InfraTrac** (counterfeit), **Innovative Biosensors** (pathogens), **InstantLabs Medical Diagnostics Corp.** (food pathogens), **NaturalCheck** (food safety), **PathSensors** (pathogens), **PlantVax** (exposure to nerve agents), **Raptor Detection** (substances), and **Smith's Detection** (chembio, radiological, nuclear, explosive detection).

The longer term threat of environmental degradation and corollary preference for products that do not pollute the air, water, or our bodies have created opportunities for biohealth entrepreneurs to find new niches and potential partners. **Bioscience International** (founded in 1994) develops environmental sampling products; **PALTIN International's** work brings new technologies to water management, **NaturalCheck's** kits and **Intralytix's** (and the late Dr. Torrey Brown's beloved) phages are finding purpose in food safety. Others, including **AquaAnimal**, **Igene Biotechnology**, **Imagilin Technology**, **MycolInnovation**, and **Plant Sensory Systems** are responding to consumer preference for reduced chemical use in raising creatures and crops for food. Still other companies are focused on technology-driven improvements to waste-to-energy and biomass-to-energy processes. They include **AH Pharma**, **Atlantic Biomass**, **Brijen Biotech**, **Clean Green Chesapeake**, **Crea-Fill Fibers** (cellulose for filtration, food, industrial, and asphalt industries) **Fiberight** (municipal solid wastes and other organic feed stock to biofuels), and **Manta Biofuel** (open water algae to crude oil). Several of the companies are located on the Eastern Shore.

## C. Wellness

Exploding markets for "wellness" products perfectly reflect the focus in medicine on preventive actions as a way to improve health and reduce health care costs, and have driven a dramatic increase in the number of Maryland companies that have entered the arena. They include **Advanced BioNutrition**, **Alpha Genix**, **Analyticon**, **Appian Medical**, **Brassica Protection Products**, **Calwood Nutritionals**, **Danya International**, **DSM Nutritional Liquids**, **GetWele Natureceuticals**, **Individualized Health Solutions**, **Mastix Medica**, **M.J. Burg & Associates**, **Nutramax Laboratories**, **Nutricia North America**, **NutriGrown**, **Nutrorganics**, and **Real Natural Remedies**.

## D. Returning veterans of new kinds of wars

The recent undeclared wars in South Asia (Afghanistan) and the Near East (ISIS) have sent combatants home with fewer head and torso injuries, but grievous harm done to their limbs, which are largely unprotected by modern body armor. Central Maryland companies are contributing advances on the field and back at home in wound care, orthopedics, tissue engineering, and regenerative medicine.

### *i. Wound care*

Maryland companies specializing in wound care include **ACell**, **Cytimmune**, **GlycoTex**, **Hollywood Oyster**, **Human Bioscience**, **Nuo Therapeutics** (FKA Cytomedix), **Osiris Therapeutics** (stem cells), **Remedium Technologies** (blood-clotting foam), **Trauma Care**, and **Weinberg Medical Physics**

### *ii. Orthopedics and prosthetics for amputees*

Maryland companies that produce orthopedics and prosthetics for amputees include **BioAccess**, **Infinite Biomedical Technologies**, and **Kinetic Revolutions**. Unfortunately, Connecticut officials successfully used funding from Connecticut Innovations to woo **Avitus** (FKA BOSS Medical), which was incubated at the ETC Eastern incubator.

### *iii. Regenerative medicine*

Regenerative medicine offers the promise of treating the root causes of many diseases, injuries and congenital conditions. It has the game-changing potential to fully heal damaged tissues and organs, offering hope to people who have conditions that today are beyond repair. Success has proven to be elusive, but advances in developmental and cell biology, immunology, and other fields have opened new opportunities to refine existing regenerative therapies and develop novel ones. “Regenerative medicine” includes a number of approaches: rejuvenation, which supports the body’s own self-healing capabilities, replacement through transplants (cell therapies) of healthy tissues or organs, and regeneration, through which specific types of cells or cell products to diseased or injured tissues or organs to eventually restore function. Maryland regenerative medicine companies (including biomaterials and tissue engineering) include: **ACell** (extracellular matrix (ECM) products to repair and remodel damaged tissues in a broad range of applications), **BioSET** (tissue repair), **CSA Medical** (cryotherapy for diseased tissue ablation), **Gemstone Biotherapeutics** (tissue engineering inventions, with a specific focus on vascularization and angiogenesis), **Mindoula Health** (tissue engineering), **Prima Therapeutics** (R&D of tissue engineering and regenerative medicine-based therapies) and **RegeneRx** (peptides that can be used in protecting, repairing, and regenerating tissue and organ damage.)

### *iv. Cell therapies*

This rapidly evolving growth area entails the administration of live whole cells or maturation of a specific cell population in a patient for the treatment of a disease, making stem cell and gene therapies special classes of cell therapies. The process starts with isolation and transfer of specific stem cell populations, administration of effector cells, induction of mature cells to become pluripotent cells, and reprogramming of mature cells. Administration of large numbers of effector cells has benefited cancer patients, transplant patients with unresolved infections, and patients with chemically destroyed stem

cells in the eye.<sup>13</sup> Maryland companies developing or using cell therapies include: AnGes (gene therapy), Cytomedix (autologous regenerative therapies company commercializing innovative platelet technologies for orthopedics and wound care), Orgenesis (cell therapies for Type 1 diabetes), Neuronascent (small-molecule therapeutic candidates that promote new neurons from the brain's own neuronal progenitor cell populations in culture and animal models), SynerGene (gene-based therapy clinical trial begun for targeted drug delivery of nanoparticle to deliver the human tumor suppressor gene p53), and **TissueGene** (optimized delivery of therapeutic proteins to repair and rebuild damaged cartilage, bone, disc, and nerve tissue for the treatment of various orthopedic diseases and degenerative disorders).

#### ***v. Stem cells***

Stem cells have the ability to differentiate themselves into many types of cells, are critical to regenerative medicine and offer radically new ways to treat and manage chronic diseases such as diabetes, heart failure and, perhaps, degenerative nerve, bone, and joint conditions. The industry was pioneered in Maryland in 1992 when Jim Burns moved the fledgling Osiris Therapeutics from Ohio to Baltimore to be nearer to Johns Hopkins' stem cell research leaders. Osiris's first product was Osteocel (cellular allograft as a bone graft substitute in spinal fusion surgery), now owned by NuVasive Inc., and its tissue engineers developed the world's first approved stem cell drug, remestemcel-L for graft versus host disease. In October 2013, Osiris sold its culture-expanded mesenchymal stem cell business, including Prochymal (remestemcel-L) and Chondrogen, to Mesoblast in a transaction worth up to \$100 million, including provision for royalty payments on future sales of products utilizing the technology. Its products now include OvationOS (a viable bone matrix designed for the filling of bony voids and to support bone repair and regeneration) as well as soft tissue solutions like Grafix® (3-dimensional matrix designed for application directly to acute and chronic wounds, including diabetic foot ulcers and burns) and Cartiform® (articular cartilage repair). Maryland stem cell therapy companies now include Cytomedix (pipeline of adult stem cell therapies for tissue repair), Lentigen (proprietary lentiviral gene delivery technology, glioblastoma, hemophilia A), MaxCyte (specialists in transfection --- the delivery of DNA or RNA into eukaryotic<sup>14</sup> cells), Retrotherapy (new technologies to better control gene expression, which may help speed the development of stem cell therapies) RoosterBio (mesenchymal stem cells from human bone marrow (hBM-MSC) for regenerative medicine research), and Stem Cell Medicine (developing stem cell therapies for neurological disorders including spinal cord injury and multiple sclerosis.)

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<sup>13</sup> American Society of Gene & Cell Therapy, [asgct.org](http://asgct.org)

<sup>14</sup> Any of various single-celled or multicellular organisms of the domain Eukaryota, characterized by cells that contain a distinct membrane-bound nucleus and by the occurrence of DNA transcription inside the nucleus and protein synthesis in the cytoplasm, in contrast to prokaryotes.



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## VI. Entrepreneurial infrastructure changes over the decade

### A. Unchanged: federal biohealth assets

First, it is important to note what has not changed: federal biohealth assets in Maryland – Centers for Medicare and Medicaid, National Security Agency, NASA, NIH,<sup>15</sup> US Army Medical Research Institute for Infectious Diseases, Walter Reed Army Institute of Research and others -- remain critical to the launch and growth of biohealth enterprises in the State of Maryland. In addition, the deep and wide cadre of contract research organizations that helped launch the industry in the state almost 40 years ago continues to grow in sophistication as the biohealth industry enters a golden age of highly individualized diagnostics and treatments. New approaches draw from the worlds of biology, information technology, nanotechnology, medicine, and engineering, giving contract engineering/manufacturing firms such as **Key Tech** an important integrative and commercialization role.

Using the three categories set out in Johns Hopkins' recent "Innovation Ecosystem" report as the armature, it is fair to assert that the entrepreneurial infrastructure in Central Maryland has progressed rapidly in the last 15 years. Beyond the familiar litany of the area's research prowess, which is largely thriving, the state has leapt to the next level in support for those who aspire to turn new knowledge into commercial and wellness success.

### B. Physical spaces for entrepreneurs have grown in number and variety

The number of traditional incubators in the region – public and private -- has increased steadily and they continue to productively graduate market-ready firms that for the most part remain in Maryland. More than numbers, however, the most striking changes have been in the morphology and functions of these "incubators." In response to market demand, they now offer shorter stays, various and often mixed spatial configurations – a desk, a cubicle, a co-working space, an office, a lab – and a variety of commercialization services at all levels of intensity and real/virtual characteristics. "Sponsored" incubators are becoming less parochial, opening their doors to other, unaffiliated short or long-term entrepreneurs, finding that the cross-fertilization is beneficial to all.

Square footage devoted to growing biohealth companies has increased exponentially. From the single location of the Maryland Technology Development Center in Montgomery County, the county's Business Innovation Network centers have grown in number and specialization. The incubator at the private nonprofit Biomedical Research Institute (BRI) in Montgomery County (originally known as the Association for Entrepreneurial Sciences, AES) has housed many of Maryland's biohealth superstars in their early days. BRI's own research focuses on schistosomiasis, and its specialized facilities and

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<sup>15</sup> For example, the former director of the National Cancer Institute, Dr. Samuel Broder, recently agreed to chair BioMarker Strategies' Scientific Advisory Board.



capabilities<sup>16</sup> have proven to be useful to its incubator tenants. With the development of its research park, bwtech@UMBC, UMBC has been able to dramatically expand its incubator opportunities for biohealth companies on the South Campus (former Martin Marietta labs, acquired by UMBC in 1996). The University of Maryland Biopark in Baltimore has been developed in the last decade, providing wet lab spaces for nascent companies, including those incubated elsewhere in the region and now needing these specialized facilities. Johns Hopkins University operates Fast Forward space at its campus in Montgomery County, on the Homewood campus, and has begun operations at a third location in East Baltimore. See Appendix A for a complete list.

### C. The supply of start-up and risk capital has grown somewhat, but...

The State of Maryland's core funding programs are only now recovering from devastating budget cuts to its technology venture funding vehicles in the 2000s. Heartening, however, has been the launch of several new programs that not only supply meaningful sums of cash but also are designed in recognition of challenges facing biohealth entrepreneurs today.

- Maryland Venture Fund back to healthier levels.
- Funding for the Maryland Industrial Partnerships Program (MIPS), one of the workhorses of biohealth technology business and product development efforts in the state is down an appalling 40% since 2009, despite fiscal impact analysis that shows that the program returns over \$30 in state revenues for every budget dollar allocated over the long term. See Appendix A for a list of companies that have benefited from the university collaborations supported by this matching-funds program.
- Restructuring of Maryland TEDCO's funding vehicles to focus on what was renamed the Technology Commercialization Fund (TCF).
- The BioMaryland Center's Biotechnology Development Awards programs offer translational, research, and commercialization phases that support the development life cycle from discovery through early production.
- The *InvestMaryland* Challenge, a national seed and early-stage business competition, awards \$100,000 grants to innovative startups. Grants are provided by the Maryland Department of Business and Economic Development's Maryland Venture Fund and the BioMaryland Center. Non-Maryland winning ventures are expected to establish a place of business in the state either through acquired space or a state incubator. At least 51% of the grant money must be spent within the state.
- One of the two purposes for which the Maryland Technology Development Corporation (TEDCO) was established in 1998 by the leadership of the General Assembly of Maryland was to assist in transferring to the private sector and **commercialize the results and products of scientific research** and development conducted by colleges and universities The new Maryland Innovation Initiative (TEDCO administered) for the first time systematically operationalizes that purpose

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<sup>16</sup>Wet lab space, autoclaves, low temp repository, AAALAC-approved Small animal facility, biohazard and chemical fume hoods, environmental rooms, and clean room facilities for GLP & GMP.

using evidence-based methods. MII was created as a partnership between the State of Maryland and five Maryland academic research institutions (Johns Hopkins University, Morgan State University, University of Maryland College Park, University of Maryland Baltimore, and University of Maryland Baltimore County.) The program is designed to promote commercialization of research conducted in the partnership universities and leverage each institution's strengths. All qualifying universities are eligible to apply for funding for Phase I and Phase II of the Program. Faculty from qualifying universities, and other entrepreneurs interested in creating a university start-up are also eligible for Phase II of the program. University start-ups are those (i) that have licensed technologies from a qualifying university within twelve (12) months of applying for an MII program award; and (ii) that are located in Maryland are eligible for Phase III funding from MII. In all phases, proposals must be directed to the commercialization of a technology or group of technologies: (i) owned by a qualifying university; (ii) disclosed to a qualifying university's technology transfer office (TTO); and (iii) for which there exists appropriate intellectual property protection. Each applicant must also work with an MII Site Miner prior to application submission. Site Miners are individuals selected by the MII program to assist start-ups and faculty in the process of submitting a strong business-oriented application, focused on commercialization.

- Biotechnology Investor Incentive Tax Credit continues to draw more interest than can be funded, despite an increase in funding in FY 2014.
- MIPS arrangement with the Maryland Department of Natural Resources has added a focus on agriculture and bio-energy companies.
- Cash awards accompanying accelerator participation.
- Both Johns Hopkins and UMD Ventures (University of Maryland College Park/University of Maryland Baltimore) have launched or are planning to launch modest investment funds.
- In FFYs 2010 and 2011, the University of Maryland System and the Army Research Laboratory established a Proof of Concept Alliance that made two rounds of commercialization awards to university or private company entrepreneurs. **GlikNik**, **Remedium**, and **Zymetis** received funding.
- BioHealth Innovation's Federal Funding Assistance Program provides technical support for preparation of applications for Small Business Innovation Research (SBIR) and Small Business Technology Transfer Program (STTR, for company/university partner applicants) funding from federal research agencies. Johns Hopkins Technology Ventures includes SBIR coaching in its menu of supports for technology commercialization.
- National Institutes of Health SBIR/STTR grantees are eligible to receive individualized help through its Commercialization Assistance Program (CAP), operated by NIH's contractor, Larta (Los Angeles). CAP is a nine-month mentoring and training program with an assigned "Principal Advisor" aimed at identifying and evaluating commercialization options and supporting the development of an 18-month market entry plan.

A few of the inventoried companies have turned to social media sources for fundraising. **Protenus** and **Quantified Care** have undertaken IndieGoGo crowd-funding campaigns, and **PapiVax** and **Gemstone**

have discovered Poliwogg and Gamma3, respectively. The Poliwogg Regenerative Medicine Fund is a business development company that invests primarily in the equity and equity-linked securities of companies involved in, or significantly benefitting from, development of drugs, devices, or treatments derived from stem cell research or other regenerative medicine technologies. The Gamma 3 Initiative was begun in 2012 and identifies, acquires and incubates high-value IP by partnering with academic institutions, inventors, and entrepreneurs.

**Vixiar Medical** received funding from Technology Venture Development (Fayetteville, AR), a virtual incubator program that provides \$250K seed money and extensive, highly structured incubation services.

## **D. An expanding array of commercialization support services**

An expanding array of commercialization support services is available to biohealth entrepreneurs, thanks in large part to major commitments by the leadership of both University of Maryland Baltimore and Johns Hopkins. See case study at the end of this section for an example.

### ***i. University commitments***

Both universities have restructured their “technology transfer” offices to focus on venture creation and are thoughtfully assembling the internal and external resources needed to support not just the licensing and commercialization of new technologies but also the creation and growth of new enterprises. In this, Hopkins has far greater flexibility than the state institution and in all probability access to far greater private financial support. But about the core functions required, the two schools agree. In addition to money, they call for initiatives that in various ways build beneficial relationships for entrepreneurs. Twenty of the 23 recipients of funding stimulated by the Maryland Biotechnology Investment Incentive Tax Credit in 2013 reported that they had extensive relationships with universities and federal labs in Maryland.

In addition to the venerable MIPS and TAP programs, the University of Maryland’s Maryland Technology Enterprise Institute (Mtech) now sponsors a VentureAccelerator program to mentor UMD inventors; the Start-Up Shell, a student-run nonprofit incubator; the Impact Seed Fund for students involved in student entrepreneurship programs at UMD, and the intensive DC I-Corps accelerator (see below). It has also forged an alliance with the Maryland Department of Natural Resources, which now provides funding for selected MIPS projects and Mtech’s Chesapeake Bay Seed Capital Fund.

Both Johns Hopkins and JHU (along with George Washington University and Virginia Tech) are participants in the National Science Foundation-funded DC I-Corps, which provides “real world, hands-on training on how to incorporate innovations into successful products” for teams of individuals from the capital region’s universities, federal labs, and the public (certain programs have more requirements for team members). “The goal is to create a new venture or licensing opportunity for program participants.” The program was developed, and is taught, by successful technology entrepreneurs.

## *ii. BioHealth Innovation*

BHI, a public-private partnership and not-for-profit corporation, was created in 2011 as a result of an economic development task force convened by Montgomery County Maryland's County Executive to examine how to build on the County's intrinsic resources to create more commercial opportunities in the biosciences industry. An initial investment by Montgomery County has been leveraged 9:1 with private sector, university, and federal funding. Among the private-sector contributors are MedImmune, AstraZeneca, GlaxoSmithKline, Roche, Emergent Biosolutions, Qiagen, United Therapeutics, Becton Dickinson, and Adventist Healthcare, venture capital firms New Enterprise Associates and SR One, as well as the large research universities of Johns Hopkins University and University System of Maryland

BHI functions as an innovation intermediary that translates market-relevant research into commercial success by connecting management, funding, and markets. It aims speed the commercialization of the State's vast research prowess by connecting regional innovation assets, developing an entrepreneurial talent and support pipeline, attracting funding for technology commercialization, and evaluating commercially relevant federal and university technology. Its premier programs include an Entrepreneur-In-Residence program that employs a team of six full-time industry and investor specialists who actively mentor and advise biohealth entrepreneurs in the Central Maryland region. These experienced specialists support BHI early-stage portfolio companies on product development and reaching commercial milestones. EIRs also work in partnership with local research intuitions in coaching technology development projects notably at the National Institutes of Health, Johns Hopkins University, and University System of Maryland.

## *iii. Accelerators*

In 2014, Johns Hopkins University, BioHealth Innovation, the Economic Alliance of Greater Baltimore, and the Maryland Department of Business and Economic Development collaborated to bring the successful DreamIt Health initiative to Baltimore. The University of Maryland and the Abell Foundation also joined as supporters of DreamIt Health in 2015. Through the intense 3-to-4 month program, participating companies receive seed capital up to \$300K, and access to customers, partners, investors and the extended DreamIt network including its alumni nationwide. While in cycle, DreamIt Health startups receive \$50,000 for an 8% equity stake; the remaining capital is available to companies that go on to raise follow-on funding. Additionally, startups gain coaching from exited entrepreneurs uniquely assigned to each company; numerous resources including free legal and accounting services, office space, Amazon Web Services and Google Cloud credits; entrepreneur best practices from industry thought leaders and more. All DreamIt programs end with the signature capstone, Demo Day, where companies pitch to a room full of potential customers, investors, and partners. The DreamIt program has successfully infused a whole new class of growth companies into the City of Baltimore, and has been a major success. DreamIt Health's second cohort is underway at the PowerPlant Live office space in downtown Baltimore. Class of 2014 graduates (and their "next steps") include ***Aegle***, ***Avhana Health***, ***emocha*** (Fast Forward), ***Protenus*** (The Broom Factory), ***the Smart Phone Physical***, and ***Tissue Analytics*** (from Philadelphia DreamIt).

In 2015, BioHealth Innovation has developed another health tech accelerator in Maryland, this time based in Montgomery County. With the help of local consulting firm Product Savvy and the Montgomery County Department of Economic Development, Relevant Health will have its first cohort of startup companies start the product-focused 5-month program in October, 2015. Similar to the DreamIt Health program, startups will have access to mentors, networks, and coaching that will help them to move their product and company to the next value inflection point by the end of the program. Relevant Health offers access and proximity to the unique resources located in the Montgomery County area, such as the FDA and NIH.

Other acceleration initiatives include Accelerate Baltimore (ETC); VentureAccelerator Program (Mtech, UMD); Accelerator for the Commercialization of Technology (ACT), Howard County-JHU Applied Physics Laboratory. Private efforts underway or planned include Betamore in Baltimore, which has become the hub of a new membership organization in the wake of the gbtc's demise and strong integrator of the Baltimore region's start-up support network members. Spark, Cordish Co.'s 20,000 sq. ft. collaborative workspace, has opened in the offices at Power Plant Live in downtown Baltimore where the 2015 class of DreamIt Health is being put through its paces. Kevin Plank (Under Armor)'s development group's plans for redevelopment of Port Covington includes conversion of a former bus garage into an innovation hub for craftsmen and startup companies. The Broom Factory, another flexible spaces-flexible terms development, has opened across the harbor at Canton.

#### ***iv. "Boots on the Ground"***

"Entrepreneurs in residence" programs provide live, experienced human beings to serve young companies for short or long periods. Bwtech@UMBC was the first incubator to employ entrepreneurs in residence. Both ***BeneVir*** and ***Perceptive Navigation*** have benefited from BioHealth Innovation's EIR programs. Last year Johns Hopkins Technology Ventures recruited 14 entrepreneurs to work with faculty. UM Ventures has a similar initiative.

#### ***v. Other mentors/advisors***

Members of the University of Maryland's Advisory Board and the Johns Hopkins Alliance for Science & Technology Development each meet throughout the year and combined once a year. They are pharmaceutical and biotechnology executives, medical device developers and manufacturers, and investors, including angel investors. These groups help the universities and entrepreneurs evaluate the commercial potential of new ventures.

#### ***vi. Private Business development consultants***

While not as numerous as CROs, private business development consultants play an important role in the bio-entrepreneurial infrastructure. Maryland examples include ***Biotech Resources***, ***Drug Design Partners***, ***Orion Inc.***, and ***Pacific Bridge Medical***. A specialized set of other consultants and suppliers backstops the support given at the launch of bio-enterprises, offering help in targeted market research, design and fabrication, new and used laboratory equipment and calibration services, and a virtual choir of regulatory specialists.

## **E. CROs continue to undergird biohealth company growth**

The large number and sophistication of contract research organizations (CROs) and other providers of materials and services to the developers of new biohealth innovations has for years been Maryland's bioscience long suit. Starting with Life Technologies, these companies once sold principally to the National Institutes of Health and other government and institutional research organizations. They continue to grow in number and technology advances and increasingly serve growing biohealth companies. They provide specialty services for medium size companies as well as virtual departments for newly developing companies that lack access to sophisticated equipment and technicians.

Approximately 200 of the companies inventoried perform contract research functions ranging from assays to complete clinical trials. Another 50 sell laboratory consumables and supplies. Many of them specialize, for example in supplies or services for central nervous system (CNS) research.



## **CASE STUDY: Rehabtics**

**Rehabtics offers a case study how the region's entrepreneurship infrastructure can be exploited for good.**

It was October 2011 when Xiaoxu Kang was given a tour of a company producing robotic assisted rehabilitation devices. Then a PhD student at the Johns Hopkins University with a research focus on physical rehabilitation, Xiaoxu thought that the huge robots looked impressive. However, she was also told that only the largest hospitals could afford to use such systems, which cost over \$200,000. Surprised at the high price, Xiaoxu asked what people had used in the past for self-directed home rehabilitation after suffering from neurological damage. "Basically nothing," she was told. Disappointed by the lack of effective low-cost solutions for patients to conduct guided physical rehabilitation at home over the long term, she left with lots of thoughts on her mind.

Soon after the visit, Xiaoxu learned from her parents during a weekend phone call that her uncle had suffered a stroke and that he had trouble moving his arms on one side since then. Her uncle needed guided physical therapy, but there was almost nothing available on the market to meet such urgent needs... Born in a family of life-long entrepreneurs, Xiaoxu had always been passionate about start-ups. So, she decided to take things into her own hands. Xiaoxu interviewed hundreds of therapists and clinicians and received overwhelmingly welcoming responses. With a polished concept and a basic prototype, Xiaoxu competed in the 2012 Johns Rehabtics, cont. Hopkins University Business Plan Competition and won 3rd Prize in the social enterprise track out of 36 highly competitive teams.

With warm support from Johns Hopkins School of Medicine's Department of Physical Rehabilitation and Medicine and the Department of Biomedical Engineering at the Johns Hopkins University, Xiaoxu applied for the National Collegiate Inventors and Innovators Alliance (NCIIA) E-team Grant. The NCIIA notified Xiaoxu about an interview while she was away for her honeymoon in Japan. Right after a long, sleepless international flight, she stayed up all night at her hotel to conduct the online interview with the NCIIA committee. A few months later, Xiaoxu was notified that the project was awarded an NCIIA grant. With the funding from NCIIA, she built the alpha version of the prototype with the help of a senior software engineer.

In October 2012, Xiaoxu officially founded Rehabtics LLC in Baltimore, Maryland, aiming to tackle the problems in the long-term rehabilitation field for millions of people suffering from stroke and other neurological conditions. In February 2013, Xiaoxu applied for Accelerate Baltimore program, and Rehabtics was selected out of over 120 applicants to enter the Class of 2013. Supported by the business mentors from Accelerate Baltimore, Xiaoxu recruited a highly-experienced and talented team from the industry with extensive game production experience. The team worked hard together and produced the much-improved beta version, which is ready for pilot testing in various facilities across Maryland. In March 2015, Rehabtics was chosen as a semi-finalist for the InvestMaryland Challenge. (Rehabtics website)

## Appendix A.

### Beneficiaries of Central Maryland's BioHealth Commercialization Infrastructure<sup>17</sup>

#### Incubators: Current and Former BioHealth Company Beneficiaries

##### **BioInnovation Center, UMB, Baltimore**

- Baltimore Bioworks
- eNeura
- Fyodor Biotechnologies Corp.
- Gliknik, Inc.
- Irazu Biodiscovery
- KoDiscovery
- Paragon Bioservices
- Quality Solutions
- SilcsBio
- SYSTAAQ Diagnostic Products
- Vigilant Bioservices
- Vizuri Health Sciences

##### **Biomedical Research Institute, formerly Association of Entrepreneurial Science (private), Rockville**

###### ***CURRENT TENANTS***

- Aparna Biosciences (nanobio)
  - BioInnovatise, Inc.
  - BioQuick, Corp.
  - Medcore
  - Omnia Biologics
  - Functional Genetics (2000-2008)
  - GenVen (1983-2000)
  - Intradigm (2001-2007)
  - Novavax (1991-2005), moved HQ to Belward Campus, Montgomery County in 2006
  - OriGene Technologies (1993-1995)
  - Protein Potential (2006-2007)
  - Sanaria (2003-2007)
  - Sitek Research and Development Corporation (1985-1994)
  - Univax Biologics (1988-1991)
- PAST TENANTS*** (founding-graduation dates)
- Advanced Biomimetic Sensors (2006-2009)
  - CryoBioPhysica (2005-2009)
  - Foligo Therapeutics (2007-2010)

##### **Bwtech@UMBC** (incubator on campus begun in 1989 in trailers, acquired Martin Marietta lab 1996, now South Campus of the research park)

###### **CURRENT TENANTS**

- |                          |                            |                             |
|--------------------------|----------------------------|-----------------------------|
| ▪ A'sas, Inc.            | ▪ GlycoPure                | ▪ Plant Sensory Systems     |
| ▪ Amethyst Technologies  | ▪ Grip Boost, LLC          | ▪ ProSpect Pharma           |
| ▪ Beck Radiological      | ▪ Instant Labs Medical     | ▪ Potomac Photonics         |
| ▪ Biomedica Management   | ▪ Diagnostics              |                             |
| ▪ Bioreclamation IVT     | ▪ Kydes Pharmaceuticals    | ▪ Synaptic Research LLC     |
| ▪ Cellomics              |                            |                             |
| ▪ Clean Green Chesapeake | ▪ MycoInnovation           | ▪ Ultraviolet Interventions |
| ▪ Cureveda               | ▪ MycoMed Technologies     |                             |
| ▪ Euveda Biosciences     | ▪ Ophiuchus Investments    |                             |
| ▪ GlycoMantra            | ▪ RxOS Medical             |                             |
| ▪ Fiberight              | ▪ Safe Equine Technologies |                             |

<sup>17</sup> Originally prepared in 2011 for what is now the Technology Ventures office of Johns Hopkins University by Marsha R. B. Schachtel, now MRBS LLC. Updated for this report.



ACCELERATOR (grads still receiving services)

- Athena Environmental Services, Inc.
- Aurora Analytics LLC
- Celsis In Vitro Technologies
- Next Breath LLC

GRADUATES

- InVitro Technologies (now Bioreclamation IVT, still at UMBC park)
- Noxilizer
- Profectus Biosciences (AIDS vaccine, southeast Baltimore City)
- Receptor Biology, Inc. (acquired by NEN Life Science Products Inc. in 2000)
- Valens Therapeutics, Inc

**Emerging Technology Center, Baltimore Eastern and Haven**

- |                                     |                                    |
|-------------------------------------|------------------------------------|
| ▪ Arcion Therapeutics (JHU founder) | ▪ Immunomic Therapeutics Inc,      |
| ▪ Ark Sciences LLC                  | ▪ Infinite Biomedical Technologies |
| ▪ BriJen Biotech LLC                | ▪ Pieran LLC                       |
| ▪ Cardioxyl Pharmaceuticals         | ▪ SAJE Pharma LLC                  |
| ▪ Cognapse, LLC                     | ▪ Surgi-Vision, Inc.               |
| ▪ CervoCheck LLC                    | ▪ Therataxis LLC                   |
| ▪ CSA Medical, Inc.                 | ▪ Traxion Therapeutics, Inc.       |
| ▪ Encore Path                       | ▪ Vigilant Medical                 |

GRADUATES

- A&G Pharmaceutical, Inc.(graduate), Columbia, MD
- Brassica Protection Products LLC (now part of B&D Nutritional Ingredients), Baltimore City
- Cellogenics (CRO and tools), Ijamsville
- Expression Pathology, Rockville
- FASgen (created by JHU's Albert Owens), UMB Biopark
- Genox Corporation (biomarkers of oxygen stress), Baltimore City
- Immunomic Therapeutics, Lancaster PA
- Juxtopia, Baltimore City
- MedForward (websites for physician practices), East Baltimore
- Salar (physician practice software), Baltimore City
- UPM Pharmaceuticals (created by UMD School of Pharmacy, cGMP formulation of orally-administered drugs), Baltimore
- Visicu (graduate, now Dutch-owned Philips Visicu, still in Baltimore)
- WellDoc (graduate, now in Baltimore City, chronic disease management)

**Fast Forward East, Fast Forward Homewood, Fast Forward MoCo (Johns Hopkins University)**

- |                            |                        |
|----------------------------|------------------------|
| ▪ BioSciCon                | ▪ JPLC Associates, LLC |
| ▪ emocha                   | ▪ Labyrinth Devices    |
| ▪ Gemstone Biotherapeutics | ▪ MediPost             |

- Neurotrope Bioscience
- Optical Diagnostics
- Perceptive Navigation
- Potomac Affinity Proteins
- Revolve Biotechnologies
- Sonavex
- Tissue Analytics

#### **Frederick Innovative Technology Center**

- Foxspire (biodefense software co.)
- GM Biosciences Inc.
- Innovative Biotech USA (Nigerian)
- Kempbio
- Kinetic Revolutions
- LavaAmp
- Medigen, Inc.
- Meridian BioGroup
- Prolias Technologies

#### **Howard County Center for Entrepreneurship's iCAT (Innovation Catalyst)**

- ClickMedix
- CrispTek
- NutriGrown
- Seguro Surgical

#### **Montgomery County Business Innovation Network (listing biohealth tenants only)**

##### **Germantown Innovation Center**

- Advanced Biomimetic Sensors
- CLC Bio (bioinformatics)
- Correlogic Systems
- GeneWiz, Inc.
- IOINN Laboratories
- Jupiter Bioscience
- Mosaigen
- NanoRods
- Rexahn Pharmaceuticals, Inc.
- RNL Biostar
- Stem Cell Medicine

##### **Rockville Innovation Center**

- Aparna Biosciences
- Batavia Bioservices
- Daewoong America, Inc.
- Envisionier Medical Technologies
- Keygene
- ViroDefense

##### **GRADUATES**

- Penn Diagnostics

##### **Shady Grove Innovation Center**

- Alper Biotech
- American Gene Technologies
- APC Biotechnology Services
- Arraystar
- AscentGene
- Athas Radiology
- Blue Torch Medical Technologies
- Capital Biosciences
- CC BioTech
- Celek Pharmaceuticals
- Cellex, Inc.
- Clarassance
- Cogent
- CombiMab

- FlexiSpine
- Fuzbien
- GenArraytion
- HeMemics
- Macrogen
- MarkPap Pacific
- Neodiagnostix
- Nogenix Oncology

#### GRADUATES

- 20/20 Gene Systems (Rockville)
- A.L. Tech Biomedical, Inc. (Bethesda)
- Advanced Vision Therapies (now Wellstat Ophthalmics Corp, Gaithersburg)
- AlphaGenics (Rockville)
- Ariadne Genomics (Rockville)
- Atlantic BioLabs (acquired by Stemron)
- Avalon Pharmaceutical (now Intrexon, Germantown, IP owned by Mass firm)
- Biofactura (Rockville)
- Cangen
- Canon Life Sciences
- CardioMed
- Cell Logic (now Endogeny Bio)
- Creatv Microtech
- Foligo Therapeutics
- GeneDx
- GenoQuest
- Human Science
- Immuno-Oncogenomics
- Silver Spring Innovation Center
- InfraTrac
- Repar Corporation
- Sinq Systems

- Omic Biosystems
- Rafagen
- Rana Bioscience
- Seegene
- Silbiotech
- TriStar Technology
- Validus
- Infinity Pharmaceutical
- Intronn
- Marligen Biosciences (Ijamsville, acquired 2009 by OriGene – Rockville)
- Neogenix Oncology (Rockville)
- Neurologic, Inc.
- Novatarg
- Panacea Pharmaceuticals
- ProCell
- Protiveris
- Quanta BioSciences
- Revico
- Rexahn Corp.
- Shreis Cardiotech (formerly Austin Systems)
- Synergy America
- Tengen
- Tetracore
- Therapeutic Genomics
- Therimmune Research (acquired by GeneLogic)
- Transmedix

**Technology Advancement Program, UMCP (1995)**

- Cosmos ID
- Prognosys LLC
- Remedium Technologies Inc.
- Renova Life Inc.
- Zymetis

**GRADUATES**

- Digene
- Martek Biosciences
- Neuralstem
- NovaScreen

**Technology Innovation Center, Hagerstown**

- Ambay Immune Sensors and Controls
- Luminescent MD LLC
- Nanolytics
- Protein RST
- Tox Path Specialists

## Technical Facilities and MIPS collaborations

### University of Maryland Bioprocess Scale-Up Facility

**HISTORY:** Established at UMD College Park in 1985, renovated and modernized with state grant of \$775,000 in 2004; doubled in size and expanded to Shady Grove with a Maryland Biotechnology Center grant of \$200,000 in 2010.

**CURRENT STATUS:** Operates as part of UMD's Mtech (Maryland Technology Enterprise Institute)

#### MARYLAND COMPANIES ASSISTED:

- 3-Dimension Pharmaceuticals
- Action Products, Inc. (Hagerstown)
- Advanced BioScience Laboratories, Inc. (Kensington)
- Advanced BioNutrition (Columbia)
- Athena Environmental Sciences Inc. (Baltimore)
- Atto Instruments, Inc. (Rockville)
- Brassica, Inc. (Baltimore)
- Becton Dickinson Microbiology Systems (Cockeysville)
- Bioscience Contract Production Corporation (Baltimore)
- Biosys Inc. (Columbia)
- Biospherics, Inc. (Beltsville)
- Biotechnology Research Labs, Inc. (Rockville)
- Cambrex (Walkersville)
- Cambrex (Baltimore)
- CarboMed
- Cell Trends, Inc. (Middletown)
- Chesapeake Biologicals (Baltimore)
- Chesapeake PERL (Savage)
- Chitin Works, Inc. (Cambridge)
- Claragen, Inc. (College Park)
- Crop Genetics International, Inc. (Columbia)
- Digene Corporation (Gaithersburg)
- EntreMed, Inc. (Rockville)
- Environmental Elements, Inc. (Baltimore)
- Gene Logic, Inc. (Rockville)
- Human Genome Sciences, Inc. (Rockville)
- Igen, Inc. (Rockville)
- Igene, Inc. (Columbia)
- Instrument Research Company, Inc. (Columbia)
- Innovative Biosensors (College Park)
- IOMAI (Gaithersburg)
- ISP Mineral Products, Inc. (Hagerstown)
- Kemp Biotechnologies, Inc. (Frederick)
- Life Technologies/BRL/Gibco, Inc. (Rockville)
- Magenta, Inc. (Baltimore)
- Martek Biosciences Corp. (Columbia)
- MedImmune, Inc. (Gaithersburg)
- Microbiological Associates (Rockville)
- Molecular Oncology, Inc. (Gaithersburg)
- New Earth Sciences, Inc. (Cambridge)
- Oceanix (Baltimore)
- Oncologix, Inc. (Rockville)
- Oncolmmunin, Inc. (College Park)
- Oncor, Inc. (Gaithersburg)
- Paragon Biotech, Inc. (Baltimore)
- PerImmune, Inc. (Rockville)
- Procter & Gamble (Baltimore)
- Proneuron Co. (Rockville)
- Proteinix, Inc. (Rockville)
- SRCHEM, Inc. (Elkridge)
- Ventenna Medical Systems (Gaithersburg)
- Wheaton Science

## Maryland Industrial Partnerships Program (MIPS)

Created in 1986, MIPS shares with start-up, small, and large companies the costs of technical collaborations with University System of Maryland researchers. The dates in parentheses below show that MIPS has frequently supplied the funding and research partners for early stage development. While MIPS funds companies focus on a full array of technologies, only the biohealth companies are listed below.

BIOHEALTH AWARD RECIPIENTS through Round 56, June 2015 (date of first MIPS award):

- 20/20 GeneSystems, Inc. (03)
- A&G Pharmaceutical, Inc. (05)
- Advanced BioNutrition Corp. (02)
- Advanced Biotechnologies, Inc. (88)
- Alba Therapeutics Corporation (05)
- Amplimmune (09)
- Animalgesic Labs (99)
- Aparna Biosciences (08)
- APC Biotechnology Services, Inc. (07)
- Assay Biomarker, Inc.
- Atlantic Biomass Conversions, Inc. (04)
- Audiodontics (91)
- BioFactura, Inc. (06)
- BioMat Sciences, Inc. (01)
- Bio-Quick Corporation (10)
- Brain Biosciences (2013)
- Calibrant Biosystems, Inc. (01)
- CAMBREX Bio Science
- CCC Diagnostics, LLC (07)
- Celadon Laboratories (01)
- Cellex Inc. (08)
- Cellphire, Inc. (15)
- CEL-SCI Corporation ( )
- Centrexion Corporation (15)
- Chesapeake PERL, Inc. (C-PERL) (99)
- Chondros, Inc.
- Columbia Biosciences, Inc. (09)
- ConverGene, LLC (14)
- Corridor Pharmaceuticals (10)
- CSA Medical (07)
- Cytimmune Sciences (88)
- Diagnostic anSERS, Inc. (14)
- EntreMed, Inc. (95)
- Fluid Motion LLC (14)
- Fuzbien Technology Institute (09)
- Fyodor Biotechnologies, Inc. (09)
- GenVec (03)
- Gliknik Inc. (07)
- GlycoPure (13)
- GreenSpacers, Inc. (11)
- Guilford Pharmaceuticals, Inc. (05)
- HeMemics Biotechnologies (08)
- HY-TEK Bio, LLC (11)
- Igene Biotechnology (96)
- Imagilin Technology, LLC (06)
- Infinite Biomedical Technologies (02)
- Innovative Biosensors, Inc. (04)
- InstantLabs Medical Diagnostics (12)
- Integrated BioTherapeutics, Inc. (09)
- JPLC Associates LLC (14)
- Juxtopia, LLC (08)
- LeukoSight, Inc. (07)
- Lofstrand Labs Limited (89)
- Manta Biofuel LLC (15)
- MedImmune LLC (now AstraZeneca) (92)
- MedSense LLC (14)
- MycoInnovation LLC (14)
- Nabi Biopharmaceuticals (91)
- NanoDERM Sciences (15)
- Neodiagnostix Inc. (06)
- Neuronascent, Inc. (10)
- Nutramax Laboratories (95)
- Omic Biosystems, Inc. (12)
- Opticul Diagnostics (11)
- Osiris Therapeutics, Inc. (96)

- OtoMagnetics (12)
- PathSensors (15)
- PharmAthene, Inc. (04)
- Plant Sensory Systems, LLC (11)
- Probiotix, Inc. (97)
- Profectus Biosciences, Inc. (06)
- Promogen (06)
- Pulse8 (14)
- RegeneRx Biopharmaceuticals (08)
- Remedium Technologies, Inc. (08)
- Rexahn Pharmaceuticals, Inc. (05)
- Royer Biomedical, Inc. (98)
- SAJE Pharma (13)
- SilcsBio, LLC (13)
- Sirnaomics, Inc. (09)
- Spectrum BioScience, Inc. (88)
- Sterilex® Corporation (92)
- Synaptic Advisory Partners (14)
- Telcare, Inc. (10)
- TheraCord LLC (15)
- Theradigm (07)
- Trevigen, Inc. (93)
- Vasoptic Medical (13)
- Vheda Health Corporation (15)
- WellDoc Communications, Inc. (07)
- W.R. Grace & Co. (now Grace) (89)
- Xcision Medical Systems LLC (11)
- ZuvaChem, Inc. (12)
- Zylacta Corporation (08)

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# Updated Genealogies of Central Maryland BioHealth Companies

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MRBS LLC  
2015

