



# SUPPORTING LIFE SCIENCES:

**A Look Back at BioCrossroads'  
Capital Strategy**

The year '2021' is displayed in a large, white, bold font, positioned within a hexagonal frame that is part of a larger network of hexagons and lines. The background of the bottom half of the cover is a gradient of blue and green with a hexagonal pattern and various scientific icons like an atom, a flask, and a hand holding a pipette.

**2021**



Since our founding in 2002, BioCrossroads has sought to ignite the continued growth of Indiana's robust life sciences industry. Growth is driven by innovation, and innovation is about connecting ideas with capital. And so, creating a capital strategy was necessary to strengthen our mission. Clarity of purpose is an essential ingredient, but in order to get a successful capital strategy off the ground, essential work to assemble these funds and link to experienced professionals had to be completed. To give some insight into that process, we've included a forward by David Johnson who began as a dedicated volunteer as BioCrossroads was being formed and who served as President and CEO of BioCrossroads from 2004 – 2018. In this report we look at the impact of BioCrossroads' capital strategy starting with the development of two institutional investor fund of fund vehicles – the \$73 million institutional Indiana Future Fund in 2003 and the \$58 million INext fund in 2008. In addition, we look at the BioCrossroads' Seed Fund Program totaling over \$24 million in a series of three investment funds closed in 2006, 2012, and 2018.

The impact has been impressive. Joined by the State of Indiana's Next Level Fund in 2017, these investment funds have been invested in more than 44 Indiana companies to date who have in turn raised \$1.97 billion and with reported transactions of more than \$3.5 billion. They contributed to at least two drugs that are currently on the market – Reyvow® and Emgality®, which collectively reached more than \$430 million in annual sales last year. And, following its acquisition of Endocyte, Novartis is building a 50,000 sq. ft. plant to manufacture radioligand therapies, a growing area of medicine in the treatment for diseases such as cancer.

It is said that "What Indiana Makes, Makes Indiana." With one out of every 10 jobs, \$11.4 billion annually in life sciences exports, and an annual economic impact to Indiana of \$80 billion, it is clear Indiana makes life sciences and life sciences makes Indiana. Investing in life sciences pays dividends in driving innovation that has led to treatments to improve the quality of life for Hoosiers – and people all over the world – all while driving Indiana's economy.

Continued investment by our state, our universities, and groups like BioCrossroads is a critical component. And it is an investment that pays off. This is an important and timely report. And certainly, it is appropriate here to thank those whose efforts have made it possible: The Lilly Endowment and the Richard M. Fairbanks Foundation, through generous grants to the CACP Foundation on behalf of BioCrossroads, and those who worked tirelessly to put together the BioCrossroads capital strategies and those who have served as catalysts for our innovation environment.

Thank you,



**Patricia A. Martin**  
*President and CEO*  
BioCrossroads



**Nora Doherty**  
*Senior Managing Director, Indiana Seed Funds*  
*Executive Vice President, BioCrossroads*

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**With thanks for support in  
producing the report:**

Matt Hall  
Managing Director  
Indiana Seed Funds  
BioCrossroads

Lori LeRoy  
EVP, Communications  
BioCrossroads  
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**For more information on this report please contact its author with BioCrossroads:**

**Nora Doherty, EVP Strategy [ndoherty@biocrossroads.com](mailto:ndoherty@biocrossroads.com)**

**Graphics by Ed Schneider, [ed@schneidergraphics.net](mailto:ed@schneidergraphics.net)**

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## PROLOGUE: A JOURNEY OF GOOD INTENT AND GREAT INTENTIONALITY

Now nearly 20 years in the making, the BioCrossroads track record of organizing, developing, and managing seed-stage and venture capital funds for promising Indiana-based life sciences start-up companies is truly impressive. The pages that follow, with included details showing the results and impacts of each of these funds, tell that story well.

That story is remarkable, simply because community-led efforts to start any kind of credible capital formation strategy from scratch are very hard to do. They are even harder to do successfully when it comes to actually creating companies and returning at least some capital to investors in the process.

The community volunteers who came forward as early as 2001 to form what eventually became BioCrossroads were tasked, first and foremost, with devising and then implementing a strategy that would for the first time make it at least possible for an inventor or university researcher to make a discovery and form a business around it without having to leave Indiana to find the essential initial capital to do so. Such a mission is never, of course, fully “accomplished.” But as this retrospective look makes clear, the Central Indiana landscape of opportunity capital for life sciences start-ups today is vastly different from what it was 20 years ago. BioCrossroads has made all the difference. As someone who had the privilege to be part of the community leader founding group, and then later to serve as the leader of BioCrossroads, I have gained the perspective that at least three fundamental priorities must be understood early and applied constantly for community-based venture capital strategies to have any real chance of success.

### **First, clear purpose and intentional focus.**

From the Indiana Future Fund in 2003 to Indiana Seed Fund III today, the stakeholders and professionals of BioCrossroads have insisted that the only way to drive new life sciences company formation in Indiana is to establish and manage true, market-based venture capital funds that can get companies started and attract the (many) future rounds of additional funding necessary to bring biotech innovation to success. These funds cannot be grants to advance interesting research. Nor can they be accelerators or incubators, even though these are both valuable programs in other contexts. Instead, these funds must represent true investment vehicles looking to find and advance new companies with promising biology or technology, featuring competent leadership teams. Among many other things, for BioCrossroads this has consistently meant that these funds had to maintain faithful and expertly advised sector focus--on pharmaceuticals, devices, diagnostics, or related technologies--rather than seeking to be more general “high technology” investment funds not expressly dedicated to the mission of building a center of bioscience innovation. The technologies, teams, commercialization pathways and investor expectations of start-up software or digital tech companies vs. start-up therapeutic or medical device companies are vastly different. The odds of success are long in either case. And so, the best chance for that success comes when the early-stage capital funds investing in these distinct sectors are focused appropriately--solely and expertly--on sector-specific milestones, outcomes, and leadership teams.



**Second, capable sponsors and credible development leaders to build the capital required.** Fundraising, particularly for something as inherently risky as starting life sciences companies, is a gateway challenge that often cannot be met, despite the best of intentions and diligent efforts. For any real chance of success, the community leaders embarking on a capital-formation-for-company-formation strategy need to have, among them, individuals with the relationships, business or industry credibility, investment experience and persistence to determine how best to tell the promising (but far from certain) story of what could happen with greater early-stage capital advancing innovation on the local landscape. BioCrossroads has had this advantage from the beginning as well. It has continued to be able to bring together a highly effective set of community volunteers, including industry leaders and business development experts who could make the case--to public sector, philanthropic, fiduciary and corporate decisionmakers alike--that investing in a life sciences seed capital fund (or an early stage fund-of-funds) really could make sense and even return capital in an Indiana regional economy favored with strong life sciences actors, assets and talent. Additionally, that volunteer effort has included along the way corporate business development leaders, university finance leaders, public pension fund fiduciaries, mission-driven philanthropic investors, experienced angel fund investors--and the right mix and volume of appropriately networked and experienced lawyers--to insist and ensure that BioCrossroads' capital funding strategies resulted in market-based, return-driven efforts. No one ever allowed those efforts to slide into settling for non-market, economic development funds that might initially stimulate entrepreneurial activity but could never really sustain it.

**Finally, highly capable - and investable - managers.** The Indiana Future Fund (IFF) described here came together because sophisticated corporate, public pension fund, university and philanthropic foundation investors believed in the depth and the fundamental competence of the professional management teams supplied by Credit Suisse Customized Funds Investment Group, later succeeded by Carlyle-AlpInvest. These widely varied investors knew that although this new capital strategy for Indiana had never been put together here before, these managers had considerable experience--and a track record of success--in delivering comparable programs elsewhere. So compelling was the management group that, even as IFF was just beginning to return capital to those investors, most of them came together again to launch the successor vehicle to IFF, the INext Fund.

Similarly, the State of Indiana knew that even though the impressive \$250 million Next Level Fund represented capital investment on a scale never before attempted by the State, the 50 South Capital managers chosen to run that fund had impressive--and again successful--experience in meeting the many demands of running other in-state investment funds.

And BioCrossroads, though organized as a non-profit initiative to promote and advance Indiana's life sciences sector, was extraordinarily fortunate to have on its team from the start a proven finance professional who could make these programs work: Nora Doherty. As fund manager, Nora brought substantial, direct, and recent experience in building innovative companies and working with leading venture capital firms to finance enterprise growth. As a result, for over 15 years, BioCrossroads has been able to organize and manage successive



seed fund programs and attract increasing numbers of institutional (and repeat) investors to those programs, because of the range of demonstrable skills of the funds' manager. Those skills have included capacities in building a portfolio, finding, and bringing forward best candidates for investment, actively managing portfolio management teams, and participating on start-up company boards, and delivering capital back to investors.

Certainly, the story here has had its share of serendipitous outcomes. There have been instances when events could have gone either way, but then just the right market conditions or the surprise emergence of a particularly timely and favorable therapeutic result in the clinic, led the way out of seeming failure to ultimate success. But even (and perhaps, especially) when events break right, getting to success requires a special form of intentionality and persistence. In the case of the BioCrossroads' Capital Strategy, those essential elements have been present from Day One.

A handwritten signature in black ink, appearing to read 'David L. Johnson', with a stylized, cursive script.

**David L. Johnson**

*President and CEO*

Central Indiana Corporate Partnership, Inc.

## IMPORTANCE OF CAPITAL TO INNOVATION AND ROBUST LIFE SCIENCES ECOSYSTEM

BioCrossroads was established in 2002 as a private sector-led initiative to capitalize and leverage one of the nation's leading centers for life sciences and to continue to grow and support Indiana's economy. Home to headquarters for Eli Lilly and Company, Roche Diagnostics, the Cook Group, Elanco, and Zimmer Biomet to name a few, Indiana also claims the nation's largest health information technology exchange, the country's largest school of medicine, and three major research institutions – Indiana University, Purdue University, and the University of Notre Dame.

Indiana ranks second among all 50 states – only behind California – in total exports of therapeutic, medical device, and related life sciences products. Indiana's life sciences sector is a leading economic producer for the state with over 59,000 Hoosiers employed at nearly 2,300 companies, not including healthcare delivery. With \$6.1 billion in total industry wages, the average wage per person in life sciences is more than twice that of the overall private sector in the state. In 2020, the life sciences sector had a state economic impact of \$80 billion.<sup>1</sup>

Historically driven by the presence of large companies, Indiana's life sciences cluster has trailed in those indicators, such as total venture capital invested, relating to new company growth. Like most Midwestern states, Indiana has neither a large volume of venture capital investment nor a significant number of life sciences institutional investors when compared with coastal states like Massachusetts, New York, and California. The entire Great Lakes region including Indiana,

Illinois, Ohio, Michigan, and Kentucky brought in \$24.6 billion in 1,677 companies in 2020 versus the \$118 billion in investment in 6,158 companies in California. That said, Indiana has seen steady growth in total capital invested and in new company formation.<sup>2</sup>

Because growth demands capital, since its founding in 2002, BioCrossroads has worked to connect capital to innovation so that discoveries can move from laboratory bench to patient's bedside. Through its for-profit affiliate BCI, BioCrossroads has organized two life sciences venture capital fund-of-funds – the \$73 million Indiana Future Fund in 2003 and the \$59 million INext Fund in 2009 – to capture a growing number of technology transfer and spin-out companies coming from industry and academia. BioCrossroads also supported the formation of Indiana's \$250 million Next Level Fund, an investment vehicle created by the Indiana General Assembly, and continues to serve on its advisory committee. Recognizing the need for early stage or seed stage capital, BioCrossroads began a seed fund program in 2005 with its Fund I completing its inaugural investment in 2006 followed by Fund II in 2012 and Fund III in 2018.

Investment in life sciences can be especially challenging when compared with other sectors. Operating within a highly regulated environment, life sciences innovation requires specialized talent and significant investment over a long period of time. It is a high bar for good reason as innovation must be safe and effective. It is also marked by a high failure rate. According to the Tufts Center for the Study of Drug Development, an independent,

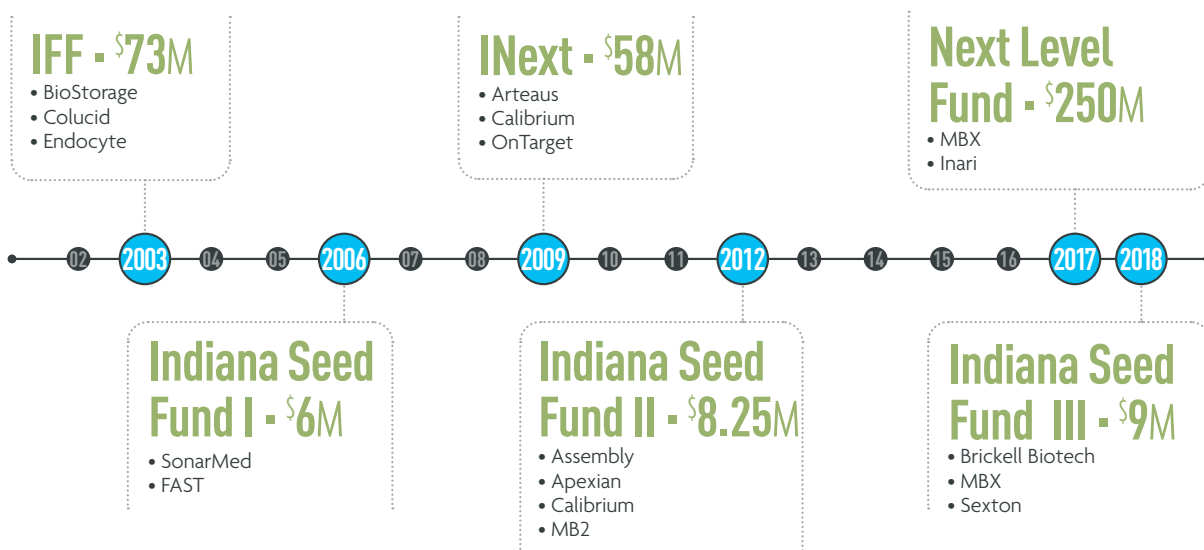
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1 Data compiled by the Indiana Business Research Center at the Indiana University Kelley School of Business and BioCrossroads. Accessed online at: [https://biocrossroads.com/wp-content/uploads/2021/04/BIOX\\_2021-IN-Life-Sci-Infographic-1.pdf](https://biocrossroads.com/wp-content/uploads/2021/04/BIOX_2021-IN-Life-Sci-Infographic-1.pdf).

2 Data pulled from Pitchbook, Accessed 21-July 15.

## BIOCROSSROADS' CAPITAL FORMATION STRATEGY

**\$200M+** Direct; **\$1.7B** in Additional Venture Capital Deployed in 44 Indiana Companies



academic, non-profit research center, it takes \$2.6 billion to develop new drugs with only 1 of 8.5 compounds in clinical development achieving approval.<sup>3</sup>

Life sciences innovation has its roots in basic research discoveries with federal funding from the National Institute of Health (NIH) providing critical resources to drive innovation. The next phase of commercialization relates to drug or prototype design followed by preclinical development and clinical trials. Many new companies are formed from technologies licensed from universities or spun-out of larger companies. Once licensed to a company, Small Business Innovation Research (SBIR) funding, state program, and university-affiliated seed funds are often sources of earliest funding. Last year, Indiana secured \$12.6 million in SBIR funding awarded to 21 companies in the area of life sciences with \$262 million Venture Capital investment in 44 companies.<sup>4</sup>

Funding innovation pays dividends for Indiana. The Fund of Funds and Seed Fund strategies implemented by BioCrossroads and supported by the many stakeholders of the life sciences community have seen positive investment returns, and more importantly, the attraction of many times that investment from capital outside the state, a growing tax base, growth of jobs, and investment in new facilities.

An overview of each fund is provided in the next section including year of operation, investors, portfolio companies, amount of leverage and summary of portfolio transactions. A summary view of the overall impact is described following. In the third section, we look for patterns in those companies that had successful exits to date. Lastly, we look forward to what comes next.

<sup>3</sup> <https://csdd.tufts.edu/csddnews/2018/3/9/march-2016-tufts-csdd-rd-cost-study> Accessed 21-June 28.

<sup>4</sup> "INDIANA LIFE SCIENCES CAPITAL: A summary of 2020 investments." Accessed online at: <https://biocrossroads.com/wp-content/uploads/2021/04/BioCrossroads-Capital-Report-2020.pdf>.

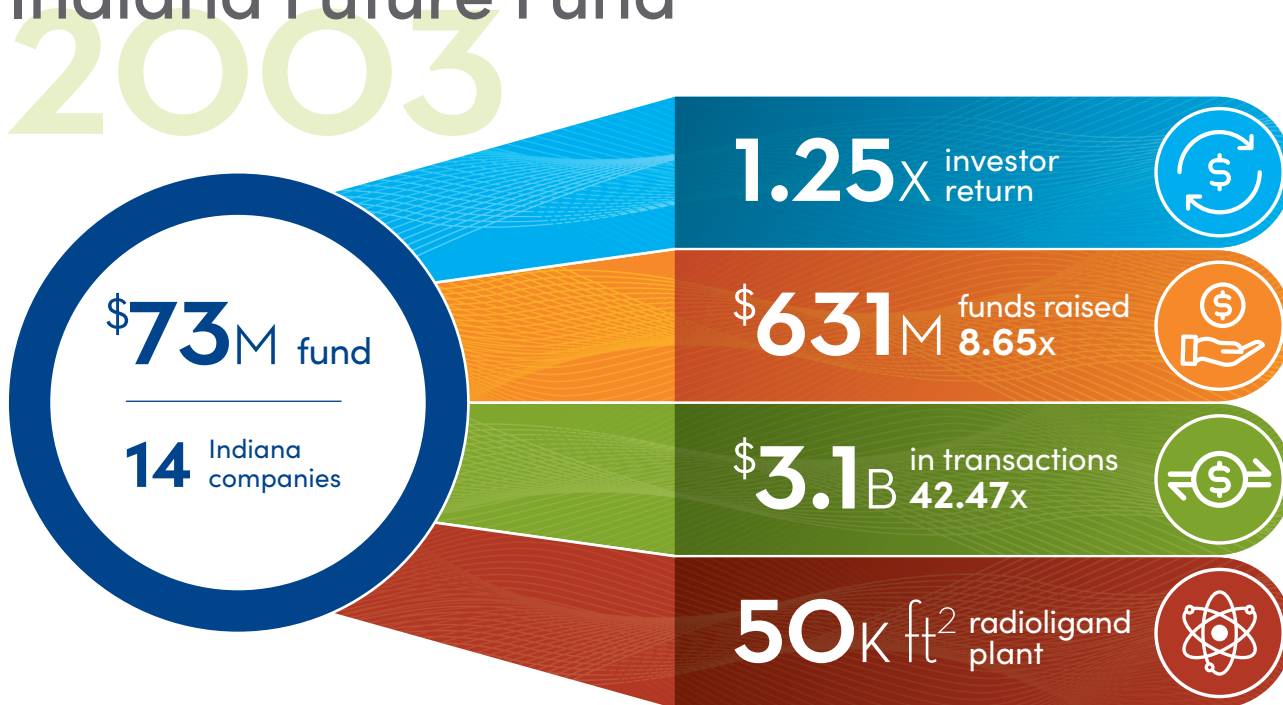
## FUND STRATEGIES – FUND OF FUNDS

### INDIANA FUTURE FUND

In 2003, as part of an overall strategy to support and grow Indiana's robust life sciences sector, BioCrossroads facilitated the creation of the Indiana Future Fund ("IFF"), a \$73 million "fund of funds" that would invest in venture funds that would, in turn, invest in opportunities to promote creation of businesses in Indiana that are on the cutting edge of biotechnology. A goal was to have 60 percent of the money, or approximately, \$44 million invested in life sciences initiative and 60 percent in Indiana companies.<sup>5</sup>

Institutional investors included Indiana's public pension funds; Indiana, Purdue, Ball State and Indiana State universities; the Indiana University Foundation; Eli Lilly and Co.; Anthem Blue Cross and Blue Shield; American United Life Insurance; and Guidant Corp.<sup>6</sup> Initially managed by Credit Suisse First Boston,<sup>7</sup> venture firms selected for the program were AM Pappas and Associates, Burrill and Company, EDF Ventures,<sup>8</sup> Pearl Street Ventures, Spring Mill Venture Partners, and Triathlon Medical Ventures.

## Indiana Future Fund



<sup>5</sup> <https://matr.net/news/indiana-future-fund-distributes-investments-4-selected-enture-capital-firms-will-back-life-sciences-efforts/> Accessed 21-May 11.

<sup>6</sup> Ibid.

<sup>7</sup> The Carlyle Group and Alpinvest assumed management of IFF in October 2013. <https://ir.carlyle.com/news-releases/news-release-details/Carlyle-group-and-alpinvest-assume-management-in-two-indiana-life/> Accessed 21-May 11.

<sup>8</sup> REI, a joint venture between Rose-Hulman Ventures in Terre Haute and EDF Ventures, based in Ann Arbor, Michigan was originally selected. Following a change at Rose-Hulman, EDF Ventures managed the investment.

## ENDOCYTE

Endocyte was formed in 1995 with technology licensed from Dr. Phil Low's lab at Purdue University.

Upon closing on a \$23M fundraising round which boosted staffing from 30 to 50-full time employees, Endocyte's CEO Ron Ellis shared that "The Future Fund was the catalyst for getting this round of financing together."<sup>1</sup>

Years later, in 2017 following disappointing data from the company's in-house drug program, CEO Mike Sherman, pivoted to outside opportunities and acquired a promising experimental drug for prostate cancer from a German chemical company.

In 2018, Novartis AG acquired the company for \$2.1 billion.<sup>2</sup>

## CO-LUCID

Co-Lucid was founded in 2005 by Indiana Future Fund investors to out-license Lasmiditan, a migraine drug first discovered by Eli Lilly and Co.

Following multiple rounds of financing, including going public in 2015, the drug was acquired by Eli Lilly in 2017 for \$960 million following publication of Phase 3 trials.<sup>3</sup>

In October 2019, the U.S. Food and Drug Administration (FDA) approved REYVOW<sup>®</sup> (Lasmiditan) an oral medication for the acute treatment of migraine, with or without aura, in adults.<sup>4</sup>

## BIOSTORAGE

Oscar Moralez and John Mills both left Covance, Inc. in 2002 to start BioStorage, a provider of sample-management services for the bioscience sector. In 2004, the company had six clients with under 50,000 samples under management. In 2007, one of the IFF funds, Spring Mill Venture Partners, invested in the company as part of an \$8.3M financing round.<sup>5</sup>

By 2010, the company appointed Greg Swanberg as CEO to succeed Mills who moved to the role of Chair, had grown to 100,000 sq. ft., and added a full-service site near Frankfurt Germany.<sup>6</sup> In November 2015, publicly traded Brooks Automation, Inc. purchased BioStorage for \$127 million representing a return of "well north of 5x" for investors. The company continues operations nearby the Indianapolis International Airport.<sup>7</sup>

1 <https://www.ibj.com/articles/11554-at-age-2-future-fund-still-work-in-progress-so-far-7-startups-have-received-investments-from-biocrossroads> Accessed 21-May 11.

2 <https://www.ibj.com/articles/73627-life-science-companies-can-learn-from-failure-if-they-stay-flexible-experts-say> Accessed 21-May 11.

3 <https://medcitynews.com/2017/01/lilly-acquires-colucid-migraine-drug/> Accessed 21-June 21.

4 <https://www.prnewswire.com/news-releases/lillys-reyvow-lasmiditan-the-first-and-only-medicine-in-a-new-class-of-acute-treatment-for-migraine-receives-fda-approval-300937322.html> Accessed 21-June 21.

5 <https://www.computerworld.com/article/2565517/turning-specimen-storage-into-a-science.html> Accessed 21-June 21.

6 <https://www.ibj.com/articles/57093-indy-life-sciences-firm-sells-for-million> Accessed 21-June 21

7 <https://www.prnewswire.com/news-releases/lillys-reyvow-lasmiditan-the-first-and-only-medicine-in-a-new-class-of-acute-treatment-for-migraine-receives-fda-approval-300937322.html> Accessed 21-June 21.

Fully invested, a total of 14<sup>9</sup> Indiana companies were reported as receiving investment by venture funds under the IFF program. These companies raised more than \$631 million in aggregate. Pitchbook, a subscription-based service reporting private and public capital market data, lists a distribution and net asset value of \$91.31 million for IFF, or 1.25 times return, as of September 30, 2020.

In addition to returns to investors, companies funded under the program have yielded substantial economic benefit to Indiana. Of the 14 companies, seven were sold, three have been dissolved, three remain operating with one having licensed technology to a public company, and one is unknown.

Financial information for each transaction is not available, but the three publicly reported transactions generated nearly \$3.1 billion in total value and each of those companies have maintained operations in Indiana.

Moreover, Novartis, the acquiror of Endocyte for \$2.1 billion in 2018, is in the process of building a 50,000 square foot advanced manufacturing plant to produce radiopharmaceuticals for cancer treatment beginning in 2023.<sup>10</sup> In total, the \$73 million IFF returned \$91.31 million to the investors in distributions and net asset value, invested in companies that raised more than \$630 million, and represented transactions totaling \$3.1 billion+ and counting – a more than 40 times return to Indiana’s economy.

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<sup>9</sup> <https://www.ibj.com/articles/15222-first-indiana-future-fund-off-to-a-slow-start> Accessed 21-May 11. It has been reported that 14 companies received investment, however a review of publications found named mention of 13.

<sup>10</sup> <https://www.ibj.com/articles/novartis-unit-to-build-plant-for-targeted-cancer-drugs-in-indianapolis> Accessed 21-May 11.



Indiana Future Fund – Indiana Portfolio Companies <sup>11</sup>						
Name and Description	Type	Est.	Raised (millions)	Sold (millions)	Disposition	
Endocyte, Developer of receptor-targeted therapeutics for the treatment of cancer and autoimmune diseases.	Life sciences – Therapeutic	1995	\$172.3	\$2,100.0	Acquired by Novartis (NYSE: NVS) for \$2.1 billion in October 2018.	
Co-Lucid, Developer of therapeutics for neurological disease including migraine headaches and pain.	Life sciences – Therapeutic	2005	\$158.7	\$960.0	Acquired by Eli Lilly (NYSE: LLY) for \$960 million in March 2017.	
BioStorage Technologies, Provider of sample-management services for the bioscience sector.	Life sciences – Services	2002	\$10.2	\$125.2	Acquired by Brooks Automation (NASDAQ: BRKS) for \$125.24 million in November 2015.	
Arxan Technologies, provider of application protection products and services.	Tech – Cyber security	2001	\$28.4	Not disclosed	Acquired by CollabNet VersionOne in April 2020.	
Cine-tal, Developer of display monitoring and color management services for digital cinema.	Tech – Entertainment	2006	\$6.22	Not disclosed	Acquired by Dolby Laboratories (NYSE: DLB) in January 2010.	
SonarMed, Developer of medical devices designed to monitor endotracheal tube position and function.	Life sciences – Medical device	2005	\$13.4	Not disclosed	Acquired by Medtronic in December 2020.	
WebLink, Provider of association management software intended to create an interactive online membership directory.	Tech – B2B software	1996	\$13.6	Not disclosed	Acquired by MemberClicks in November 2017.	
Apexian Pharmaceuticals, Developer of therapeutics for treatment of cancer using Ape1 inhibitor pathway.	Life sciences – Therapeutic	2005	\$11.8	Operating/ Licensed	Licensed ophthalmic applications to Ocuphire (NASDAQ: OCUP) January 2020.	
Quadraspec (Perfinity), Developer of consumable kits and automated healthcare instrument solutions.	Life sciences – Diagnostic	2004	\$30.6	Operating	Operating	
Scale Computing, Developer of cloud-based data storage platform intended to automate data management.	Tech – B2B	2007	\$173.6	Operating	Operating	
CS Keys, Developer of cancer-specific proteomics for diagnostic and therapeutic application.	Life sciences – Diagnostic	2006	\$13.9	Dissolved	Dissolved 2011	
FlowCo, Developer of diagnostic medical devices designed to offer treatment of flow pathologies.	Life sciences – Diagnostic	2007	\$3.5	Dissolved	Dissolved 2020	
Muroplex, Developer of therapeutic for autoimmune related diseases.	Life sciences – Therapeutic	2005	\$1.0	Dissolved	Dissolved 2015	

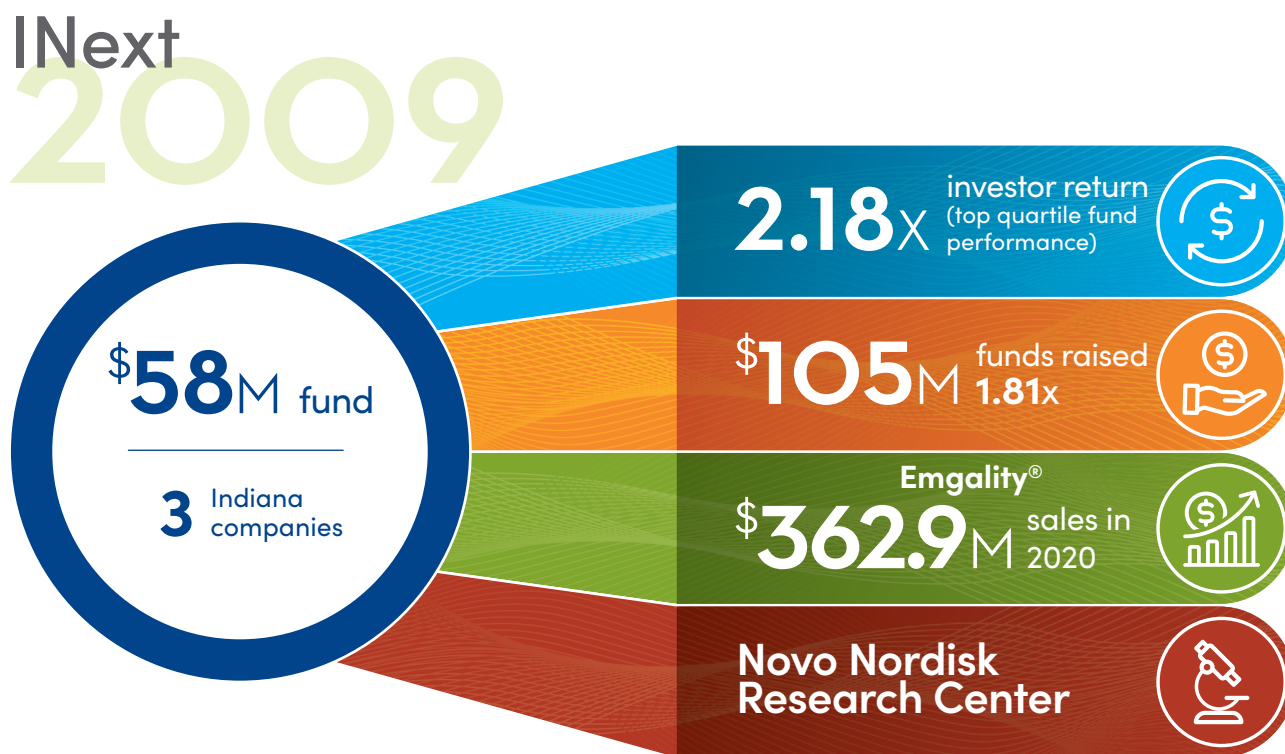
<sup>11</sup> Information from 13 identified companies from Pitchbook, Accessed 21-May 12.

## INEXT

Capitalizing on the continued strong growth of Indiana's life sciences industry and successful "fund of funds" strategy with Indiana Future Fund, BioCrossroads facilitated the creation of the INext Fund ("INext") in 2009. This \$58 million "fund of funds" was designed to invest in venture funds that were focused on life sciences opportunities. INext closed at a time when there had been a substantial contraction in the number of venture funds resulting in fewer, larger funds with a national focus which was reflected in venture funds participating in the program. One

Investor commented "Indiana's robust life sciences industry is one of the key drivers of our economy and investing in INext is expected to deliver investment returns by capitalizing on that strength."<sup>12</sup>

Institutional investors included Eli Lilly and Co.; Indiana State Teachers' Retirement Fund; Indiana University; Purdue University; University of Notre Dame; and Richard M. Fairbanks Foundation.<sup>13</sup> Initially managed by Credit Suisse First Boston,<sup>14</sup> venture firms selected for the program were 5AM Ventures, HIG BioVentures, Orbimed Advisors, SV Life Sciences, and Clarus Ventures.



<sup>12</sup> <https://www.venturecapitaljournal.com/inext-fund-forms-with-58-million/> Accessed 21-May 17.

<sup>13</sup> Ibid.

<sup>14</sup> The Carlyle Group and Alpinvest assumed management of IFF in October 2013. <https://ir.carlyle.com/news-releases/news-release-details/carlyle-group-and-alpinvest-assume-management-two-indiana-life> Accessed 21-May 11.

## ARTEAUS

Arteaus was founded in 2010 by Atlas Venture Development Corp (AVDC) and INext Fund's Orbimed Advisors to out license the anti-CGRP antibody from Eli Lilly and Co for migraine prevention.

With a very compelling hypothesis in migraine prophylaxis, funding was raised to support a 200+ patient Phase 2a proof of concept study.<sup>1</sup>

In approximately 2.5 years, the program moved from an IND to a completed Phase 2 with Eli Lilly regaining control of the drug in 2014. The experimental antibody eventually become Emgality®. According to Atlas, "based on public disclosures, [Arteaus] earned more than \$300 million in payment across upfront, milestones and royalties."<sup>2</sup>

## CALIBRIUM

In 2012, well-known biotech inventor and serial entrepreneur, Dr. Richard DiMarchi, was joined by Fritz French to form Calibrium to develop protein-based drugs to treat diabetes and related metabolic diseases. DiMarchi also formed MB2 shortly thereafter.

Working together again following success with Marcadia Biotech which was sold to Roche in 2010, Calibrium was sold to Novo Nordisk in 2013 for an undisclosed amount after raising just \$1.7 million.<sup>3</sup>

## ON TARGET LABS

On Target Labs was founded in 2010 to develop technology licensed from the lab of Dr. Philip S. Low, Purdue University. A fluorescent imaging technology designed to target and illuminate cancer during surgery, it has the potential to reduce uncertainty associated with finding and removing diseased tissue during medical procedures.

HIG BioVentures first invested in the company in 2018 and again participated in a follow on investment in March 2021 to support development and commercialization activities. The Company has a New Drug Application (NDA) under priority review by the US Food and Drug Administration.<sup>4</sup>

1 <https://www.forbes.com/sites/brucebooth/2014/01/13/the-arteaus-therapeutics-story-rd-externalization-with-eli-lilly/?sh=7c8751127667> Accessed 21-May 14.

2 <https://www.biopharmadive.com/news/atlas-venture-caps-superb-venture-return-on-arteaus-with-260m-royalty-sa/551733/> Accessed 21-June 22.

3 <https://www.ibj.com/articles/54632-novo-nordisk-buying-2-dimarchi-launched-drug-firms> Accessed 21-June 22.

4 <https://www.prnewswire.com/news-releases/on-target-laboratories-secures-21-million-for-development-and-commercialization-of-pafolacianine-sodium-injection-301254722.html> Accessed 21-June 22.

Fully invested, a total of three Indiana companies were reported as receiving investment by venture funds under the INext program. These companies have raised more than \$105 million in aggregate to date. Pitchbook, a subscription-based service reporting private and public capital market data, lists a distribution and net asset value of \$126.5 million for the Fund, or 2.18 times return, as of September 30, 2020.

In addition to returns to investors, companies funded under the program have yielded substantial economic benefit to Indiana. Through Arteaus, Eli Lilly and Co. advanced an experimental antibody which would eventually become Emgality®. In 2020, sales of this drug were \$362.9 million up from \$162.5 million in 2019.<sup>15</sup> Following the acquisition of Calibrium in 2014, Novo Nordisk established its Indianapolis Research Center located at Purdue Discovery Park. Joining

centers in Seattle, Boston, and Fremont, CA, the Indianapolis Research Center is “home of an elite research team contributing to Novo Nordisk’s global research efforts focused on early discovery projects within the diabetes and obesity areas.”<sup>16</sup> The third company, On Target Labs, remains independent and is completing its Phase 3 clinical trial, ELUCIDATE, evaluating the effectiveness of the candidate to intraoperatively identify lung cancer in real-time.

The \$58 million INext Fund returned \$126.5 million to the investors in distributions and net asset value, invested in companies that raised more than \$105 million, yielded a new treatment for migraine which posted sales of \$362.9 million in 2020, added a research site for a global pharmaceutical company, and supported the ongoing development of a technology to target and illuminate cancer during surgery.

INext – Indiana Portfolio Companies <sup>17</sup>					
Name and Description	Type	Est.	Raised (millions)	Sold (millions)	Disposition
Arteaus, Developer of antibody to calcitonin gene-related peptide (CGRP) for the prevention of migraine headaches.	Life sciences – Therapeutic	2011	\$18.0	Not disclosed	Acquired by Eli Lilly (NYSE: LLY) for an undisclosed amount in December 2013. <sup>18</sup>
Calibrium, Developer of therapeutics for the treatment of diabetes and related metabolic diseases.	Life sciences – Therapeutic	2012	\$1.5	Not disclosed	Acquired by Novo Nordisk (CSE: NOVO B) for an undisclosed amount in August 2015.
On Target Laboratories, Developer of a fluorescent imaging technology designed to target and illuminate cancer during surgery.	Life sciences – Diagnostic	2010	\$85.2	Operating	Phase 3 Trial, ELUCIDATE, ongoing

<sup>15</sup> <https://www.prnewswire.com/news-releases/lilly-reports-strong-fourth-quarter-and-full-year-2020-financial-results-301217838.html> Accessed 21-June 22.

<sup>16</sup> [https://www.novonordisk-us.com/content/dam/nncorp/us/en\\_us/homepage/about-us/who-we-are/pdf/US%20Research%20Fact%20Sheet%202020.pdf](https://www.novonordisk-us.com/content/dam/nncorp/us/en_us/homepage/about-us/who-we-are/pdf/US%20Research%20Fact%20Sheet%202020.pdf) Accessed 21-June 22.

<sup>17</sup> Information from 13 identified companies from Pitchbook, Accessed 21-May 12.

<sup>18</sup> Atlas, an investor in Arteaus said that, based on public disclosures, the biotech reaped more than \$300M in payments across upfront, milestones and royalties. <https://www.biopharmadive.com/news/atlas-venture-caps-superb-venture-return-on-arteaus-with-260m-royalty-sa/551733/> Accessed 21-June 22.



## NEXT LEVEL FUND

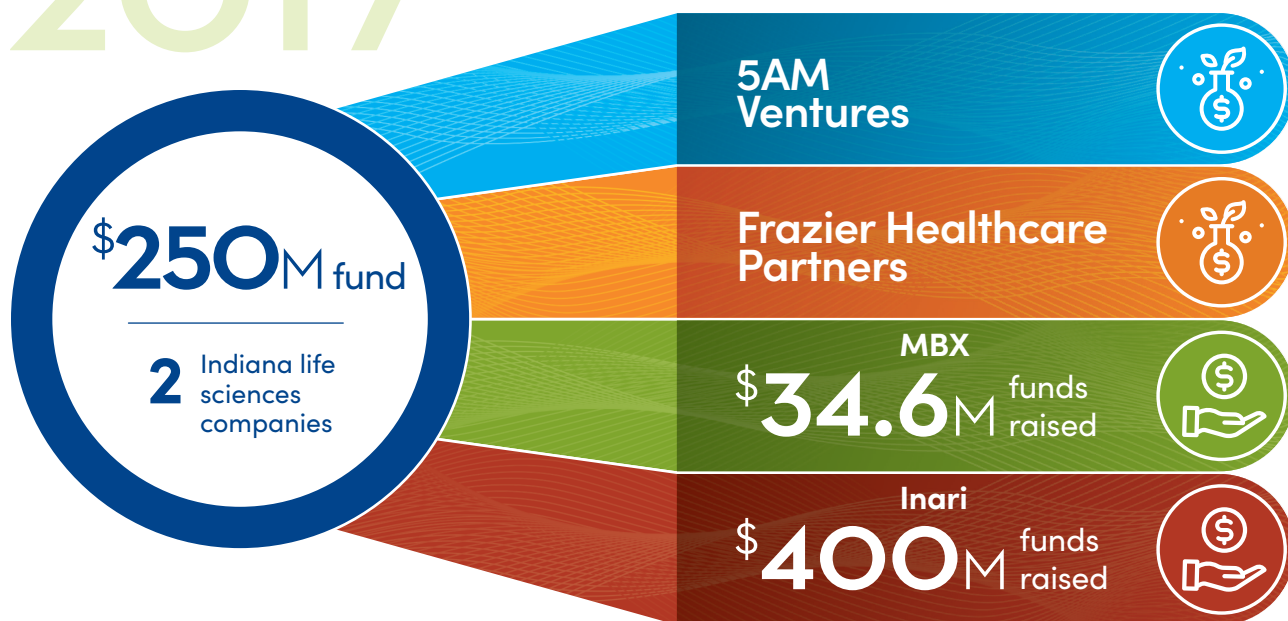
In 2017, under Governor Holcomb's leadership the Indiana General Assembly created the Next Level Fund ("NLF") using \$250 million from the 2006 lease of the Indiana Toll Road to "make targeted investments in Indiana venture capital funds and businesses to generate competitive investment performance and support increased innovation and entrepreneurship in the State."<sup>19</sup>

Focused on technology, the fund supports innovation in Indiana's traditional sectors of advanced manufacturing, life sciences, information technology, distribution, and agriculture. Managed by 50 South Capital,

NLF has invested in a number of venture firms including two life sciences venture firms with a demonstrated practice of investing in Indiana life sciences opportunities: 5AM Ventures and Frazier Healthcare Partners. In addition, the Fund has made an investment in Inari through Acre Venture Partners.

The Fund is still within its investment period and no return information is available via Pitchbook. However, Indiana has already received economic benefit from the Fund. The investment in Frazier Healthcare Partners was quickly deployed into an investment in MBX which closed on a \$34.6 million raise in July 2020. BioCrossroads' Seed Fund also participated in this round. In 2021, 5AM

## Next Level Fund 2017



<sup>19</sup> <https://www.nextlevelindianafund.com/overview> Accessed 21-June 22.

Ventures joined Next Level Fund as the second life sciences venture firm in the program. With a demonstrated track record of investment in Indiana life sciences companies, including Calibrium under the INext program, 5AM Ventures is well positioned to support opportunities in the State.

The Next Level Fund is also invested in agriculture focused life sciences company,

Inari, through Acre Ventures. Inari was founded in 2016 and has operations in Boston, MA; West Lafayette, IN; and Belgium. Pitchbook reports \$400M in total funds raised to date and a \$1.21 billion valuation. A developer of a plant breeding platform designed to build a more sustainable food system, approximately half of its 180 employees are located in West Lafayette, IN at the Purdue Research Park.

Next Level Fund Table <sup>20</sup>					
Name and Description	Type	Est.	Raised (millions)	Sold (millions)	Stage
Inari, Developer of plant breeding platform designed to build a new and more sustainable food system.	Life sciences – AgTech	2016	\$400.0	Operating	Active trials in gene editing for seeds in multiple crops
MBX Biosciences, Developer of therapeutics for treatment of endocrine diseases.	Life sciences – Therapeutic	2018	\$34.6	Operating	Pre-clinical

<sup>20</sup> Information from two identified companies from Pitchbook. Accessed 21-June 22.



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## MBX

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MBX was founded in 2018 to develop therapeutics licensed from Dr. Richard DiMarchi's lab at Indiana University for treatment of endocrine diseases.

Kent Hawryluk and Timothy Knickerbocker joined Dr. DiMarchi, a veteran of multiple successful drug development programs, as co-founders.

In July 2020, Frazier Healthcare Partners was the lead for a \$34.6 million funding round joined by national firms New Enterprise Associates and OrbiMed as well as BioCrossroads and IU Ventures.

Funding will be used to support the company's preclinical pipeline of peptide therapeutic candidates.<sup>1</sup>

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1 Pitchbook. Accessed 21-June 22.

2 <https://www.purdue.edu/newsroom/releases/2018/Q4/inari-introduces-worlds-first-seed-foundry-leaps-from-boston-to-purdue-research-park-with-goal-to-transform-agriculture.html> Accessed 21-June 22.

3 <https://inari.com/news/inari-raises-over-200-million-to-unlock-the-full-potential-of-seed> Accessed 21-June 22

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## INARI

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Inari, based in Cambridge, Massachusetts, was founded in 2016 by Flagship Pioneering to build a new, more sustainable food system. In 2018, the company opened a location at Purdue Research Park to support product development and innovation and take advantage of proximity to Purdue's College of Agriculture as well as seed companies.<sup>2</sup>

Since then, operations in West Lafayette have grown such that approximately half of Inari's 180 employees are based in Indiana. The company announced a raise of \$208 million in May 2021.<sup>3</sup>

## FUND STRATEGIES – BIOCROSSROADS' SEED FUNDS

### INDIANA SEED FUND I

In 2005, just two years following the formation of the Indiana Future Fund, BioCrossroads established the Indiana Seed Fund I ("ISFI") to make early-stage investments in life sciences companies. A return-driven vehicle, ISFI was focused on making direct equity investments that would preserve the companies' ability to raise future funds from traditional sources in companies with a focus on technology commercialization and validation in the areas of life sciences (not basic research). ISFI was targeted to invest in approximately 10 companies with initial investments ranging from \$250K to \$500K with investments structured and overseen in the best way to ensure eventual market success for its portfolio companies and their founders. ISFI's broader objective was to jump-start the new company formation process in Indiana's conventional, more institutional environment through an investment strategy that would

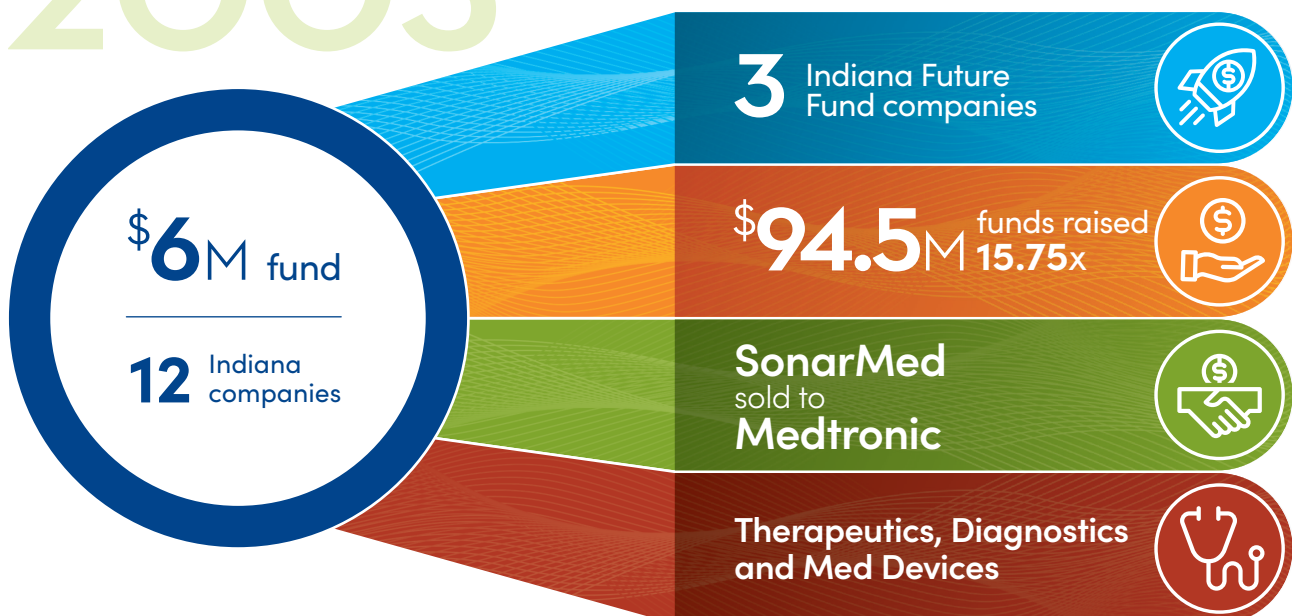
pay strong attention to advancing promising innovation but also insist (and help) company founders go the distance to ensure that their innovation could achieve commercial and clinical success.

Investors included BC Initiative, Inc., the for-profit arm of BioCrossroads, and two State of Indiana vehicles that were under the direction of the Indiana Finance Authority (IFA) and the Indiana Economic Development Corporation (IEDC).

Fully invested, ISFI has made investments in 12 companies which have raised more than \$94.5 million in equity as of mid - 2021 representing more than 15 times the investment made by the Fund.

In addition to returns to investors, the Fund succeeded in unlocking considerable new (and lasting) entrepreneurial activity and talent; spurred the participation of significant

## Indiana Seed Fund I 2005



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## SONARMED

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Founded in 2005, SonarMed developed a sound-based technology called the AirWave™ Airway Monitoring System to solve critical airway management challenges. AirWave provides continuous, real-time endotracheal tube monitoring and is indicated for both neonatal/pediatric and adult use. It is the only FDA cleared airway monitoring system for patients who can't breathe on their own.

The AirWave technology was initially developed at Purdue University by SonarMed founders Dr. Jeffrey Mansfield, Dr. Eduardo Juan, and Dr. George Wodicka, using the principles of acoustic reflectometry to develop a more comprehensive approach for the management of endotracheal tubes.<sup>1</sup> Other key members included CEO, Tom Baumgardner; CFO, Dave Gunn; VP, Laura Lyons; and Director, Sven Schreiber.

ISFI's first investment in 2006, the Fund had active engagement with the Company and held board director and observer positions up until the sale of the Company to Medtronic in 2020.

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## ZORION

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Founded in 2011, Zorion is developing fully absorbable devices, including stents, from novel medical alloys.

Prototypes have been developed and tested across a range of sizes and specifications. Multiple pre-clinical studies have demonstrated safety and efficacy of the technology. First clinical application targets the growing problem of dissections in peripheral artery disease. David Broecker is the founder and executive chair.<sup>2</sup>

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## AGENEBIO

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Founded in 2008, AgeneBio is developing a therapeutic to preserve and restore cognitive function for amnesic mild cognitive impairment (aMCI), the symptomatic pre-dementia stage of Alzheimer's disease. Licensed from Dr. Michela Gallagher's lab at Johns Hopkins, the management team at the time of the Fund's investment was based in Indiana.

The Company announced completion of patient enrollment in Phase 2B clinical trial to treat Amnesic Mild Cognitive Impairment due to Alzheimer's Disease with topline results expected in November 2022.<sup>3</sup>

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## FAST BIOMEDICAL

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Founded in 2006, FAST BioMedical is designing technologies to advance heart failure treatment through more precise measurement of volume status and kidney function. The technology was licensed from Dr. Bruce Molitoris' lab at the Indiana University School of Medicine. Leadership of the company also includes Joe Muldoon, CEO; Jim Strickland, VP and co-founder, and Trey Putnam, VP.

A clinical stage company, results from a recent heart failure study demonstrating the utility of its technology were published in the European Society of Cardiology (ESC) Heart Failure Journal. An open-label study using its technology in chronic dialysis patients was completed in May 2021.<sup>4</sup>

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1 <https://www.sonarmed.com/about-us/> Accessed 21-June 25.

2 <http://www.zorionmedical.com/home.html> Accessed 21-June 25.

3 <https://agenebio.com/agenebio-announces-completion-of-patient-enrollment-in-phase-2b-clinical-trial-to-evaluate-agb101-to-treat-amnesic-mild-cognitive-impairment-due-to-alzheimers-disease/> Accessed 21-June 25.

4 <https://www.fastbiomedical.com/news> Accessed 21-June 25.

additional investors, including angel investors; and forged invaluable relationships both with Indiana's research universities, and also with the State of Indiana around promising life sciences sector investment opportunities.

ISFI's first investment in 2005 was made in SonarMed, a developer of technology

licensed from George Wodicka's lab at Purdue University to monitor endotracheal tube position and function, was sold to Medtronic in December 2020. Four of the portfolio companies have been dissolved and the remainder are continuing to pursue commercialization. Selected companies are highlighted below.

Indiana Seed Fund I Portfolio Companies <sup>21</sup>					
Name and Description	Type	Est.	Raised (millions)	Sold (millions)	Disposition
SonarMed, Developer of medical device to monitor endotracheal tube position and function.	Life Sciences – Medical Device	2005	\$13.4	Not disclosed	Acquired by Medtronic (NYSE: MDT) for an undisclosed amount in December 2020.
AgeneBio, Developer of therapeutics for treatment of aMCI and other neurological and psychiatric diseases.	Life sciences – Therapeutic	2008	\$13.4	Operating	Clinical
ARP, Developer of medical device for cardiac applications.	Life sciences – Medical Device	2008	\$1.1	Operating	Pre-clinical
FAST BioMedical, Developer of more precise measurement of volume status and kidney function.	Life sciences – Diagnostic	2006	\$33.8	Operating	Clinical
GRest, Developer of medical device intended to support weight-loss procedures.	Life sciences – Medical device	2007	\$5.0	Operating	Pre-clinical
Pericardial Access, Developer of device for treatment of cardiac disease.	Life Sciences – Medical Device	2008	\$1.1	Operating	Pre-clinical
Zorion, Developer of resorbable devices, including stents.	Life Sciences – Medical Device	2011	\$1.1	Operating	Pre-clinical
ImmuneWorks, Developer of therapeutics for treatment of lung disease.	Life sciences – Therapeutic	2006	\$11.7M	Licensed	Licensed to Magnolia Tx
Aarden Pharmaceuticals, Developer of small molecule drugs for the treatment of infectious diseases, cancer, metabolic and autoimmune conditions.	Life sciences – Therapeutic	2008	\$1.8	Dissolved	Dissolved 2015
Bioscience Vaccines, Developer of vaccine adjuvant.	Life sciences – Therapeutic	2009	\$0.6	Dissolved	Dissolved 2016
CS-Keys, Developer of cancer-specific proteomics for diagnostic application.	Life sciences – Diagnostic	2006	\$13.9	Dissolved	Dissolved 2011
FlowCo, Developer of diagnostic to offer treatment of flow pathologies.	Life sciences – Diagnostic	2007	\$3.5	Dissolved	Dissolved 2020

<sup>21</sup> Information from portfolio companies from Pitchbook. Accessed 21-May 12.



## INDIANA SEED FUND II

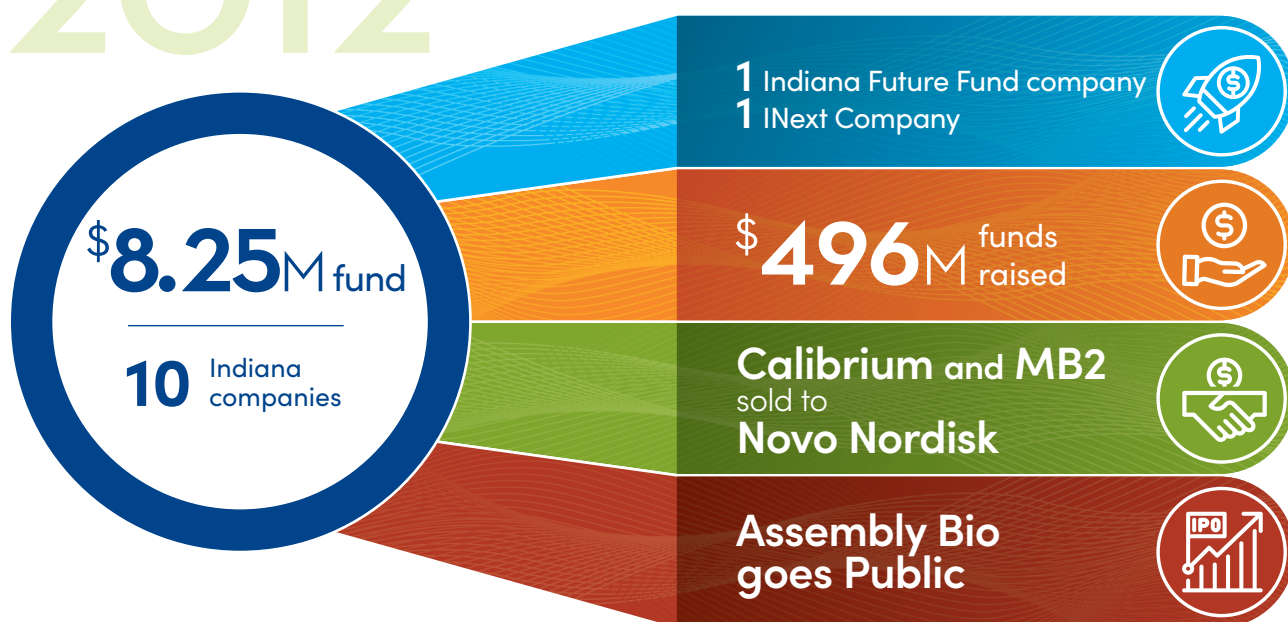
Following on the full deployment of ISF1, BioCrossroads announced the formation of the \$8.25 million Indiana Seed Fund II (“ISF2”) in 2012. An early-stage capital fund focused on identifying, creating and developing the next generation of Indiana-based life sciences companies, ISF2 planned to invest \$500 thousand on average, in early-stage biotechnology, pharmaceutical, medical device, diagnostic, ag-biotech and health information technology products and platforms, continuing BioCrossroads’ focus on promising companies formed around innovative ideas. A return-driven vehicle, ISF2 sought to invest in early-stage life sciences companies progressing towards defined milestones to secure a Series A financing, strategic partnership or co-development agreement. Companies must illustrate proven management teams, owned or licensed technology, intellectual property, and a demonstrable and validated market need.

Investors included BC Initiative, Inc., the for-profit arm of BioCrossroads, Eli Lilly and Company, the Richard M. Fairbanks Foundation, Indiana University Research and Technology Corporation, Purdue University, the University of Notre Dame, and WellPoint.<sup>22</sup>

Fully invested, ISF2 completed investments in 10 companies which have raised more than \$496 million in equity as of mid - 2021 representing more than 60 times the investment made by the Fund.

In less than three years after making its first investment, the ISF2 realized a positive return when Novo Nordisk purchased Calibrium and MB2 (both of which are described in the box below) for an undisclosed amount in 2015. The year prior, in 2014, Assembly Biosciences completed a reverse merger into Ventrus Biosciences resulting in the Fund holding shares publicly traded on Nasdaq (ASMB). Following

## Indiana Seed Fund II 2012



<sup>22</sup> <https://medcitynews.com/2012/04/biocrossroads-forms-indiana-seed-fund-ii-for-early-stage-life-science-companies/>

Accessed 21-June 25.

a usual and customary lock up period, the Fund was able to liquidate shares on the public market. Assembly Biosciences has raised over \$400 million to advance therapies for the treatment of Hepatitis B with multiple candidates in clinical trials. Another portfolio company, Apexian, licensed technology in January 2020 to Ocuphire (Nasdaq: OCUP). A clinical trial for ophthalmic indications is currently underway.

In addition to returns to investors, the ISF2 has continued its strong partnerships with other early-stage life sciences sector investors including Elevate Ventures, University

sponsored investment vehicles at Indiana University and Purdue University, and later stage investors including 5AM, Frazier Healthcare Ventures, and Pearl Street Ventures.

Portfolio companies such as Diagnotes and SpeechVive are impacting the lives of patients in a positive way. Diagnotes is used by physicians at IU Health to make notes on patient care and supports telehealth visits. The SpeechVive device has helped hundreds of patients suffering from Parkinson's Disease to speak louder and more clearly.

Indiana Seed Fund II Portfolio Companies <sup>23</sup>					
Name and Description	Type	Est.	Raised (millions)	Sold (millions)	Disposition
Calibrium, Developer of therapeutics for the treatment of diabetes and related metabolic diseases.	Life sciences – Therapeutic	2012	\$1.5	Not disclosed	Acquired by Novo Nordisk (CSE: NOVO B) for an undisclosed amount in August 2015.
MB2, Developer of therapeutics for the treatment of diabetes and related metabolic diseases.	Life sciences – Therapeutic	2014	\$1.5	Not disclosed	Acquired by Novo Nordisk (CSE: NOVO B) for an undisclosed amount in August 2015.
Assembly Biosciences, Developer of therapies for treatment of Hepatitis B virus (HBV).	Life sciences – Therapeutic	2012	\$441.0	Operating/ Nasdaq: ASMB	Clinical
Apexian Pharmaceuticals, Developer of therapeutics for treatment of cancer using Ape1 inhibitor pathway.	Life sciences – Therapeutic	2005	\$11.8	Operating/ Licensed	Licensed ophthalmic applications to Ocuphire (NASDAQ: OCUP) January 2020.
Allinaire Therapeutics, Developer of therapeutics for treatment of pulmonary diseases.	Life sciences – Therapeutic	2011	\$1.8	Operating	Pre-clinical
Anagin, Developer of therapeutics for treatment of neuropsychiatric disorders.	Life sciences – Therapeutic	2013	\$4.4	Operating	Pre-clinical
Diagnotes, Developer of online healthcare platform.	Life Sciences – Technology	2010	\$6.9	Operating	Revenue
SpeechVive, Developer of smart ear device to help in communication.	Life sciences – Medical Device	2013	\$4.7	Operating	Revenue
Algaeon, Developer of algae cultivation platform.	Life Sciences – Agriculture	2008	\$4.8	Dissolved	Dissolved 2018
Esanex, Developer of therapeutics for cancer using HsP90 pathway.	Life sciences – Therapeutic	2011	\$18.1	Dissolved	Dissolved 2021

<sup>23</sup> Information from portfolio companies from Pitchbook. Accessed 21-May 17.



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## ASSEMBLY BIOSCIENCES

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Discoveries by leading Hepatitis B Virus (HBV) investigator, Dr. Adam Zlotnick, Indiana University, led to the formation of Assembly Biosciences (Nasdaq: ASMB) in 2012. A clinical-stage biotechnology company developing innovative therapeutics targeting HBV by focusing on advancing a new class of potent, oral core inhibitors that have the potential to increase cure rates for chronically infected patients.

HBV is a global epidemic that affects more people than Hepatitis C Virus (HCV) and HIV infection combined—with a higher morbidity and mortality rate. HBV is a leading cause of chronic liver disease and need for liver transplantation, and up to one million people worldwide die every year from HBV-related causes.

ASMB has multiple compounds in clinical trials and licensed additional technology in November 2020 from Dr. Zlotnick's lab.<sup>1</sup>

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## CALIBRIUM & MB2

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In 2015, Novo Nordisk purchased two Indiana companies developing therapeutics to treat diabetes and other metabolic diseases. Both were based on technology developed by Dr. Richard DiMarchi, a world leading peptide chemist, former executive at Eli Lilly and Company, and current professor at Indiana University.

DiMarchi was joined by co-founder Fritz French to form Calibrium in 2012 and co-founder Kent Hawryluk to form MB2 in 2014. Both had worked with DiMarchi at Marcadia which was sold to Roche in 2010 for a minimum of \$287 million. The purchase price for Calibrium and MB2 was undisclosed, however just \$3 million combined was raised prior to the sale.<sup>2, 3, 4</sup>

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## APEXIAN

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Apexian was founded in 2005 following the discovery and characterization by Dr. Mark Kelley at IU Simon Cancer Center of the APE1/Ref-1 target and its mechanisms. He led the team that identified a compound, APX3330, which was initially tested in advanced solid tumors. More recent presentations have demonstrated utility in ophthalmic and other clinical indications.

In 2020, this program was licensed to Ocuphire (Nasdaq: OCUP) for all ophthalmic and diabetic indications. Clinical trials are currently underway.<sup>5</sup>

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- 1 <https://investor.assemblybio.com/news-releases/news-release-details/assembly-biosciences-and-door-pharmaceuticals-sign-collaboration> Accessed 21-June 25.
  - 2 <https://www.ibj.com/articles/54632-novo-nordisk-buying-2-dimarchi-launched-drug-firms> Accessed 21-June 22.
  - 3 <https://www.purdue.edu/newsroom/releases/2018/Q4/inari-introduces-worlds-first-seed-foundry-leaps-from-boston-to-purdue-research-park-with-goal-to-transform-agriculture.html> Accessed 21-June 22.
  - 4 <https://inari.com/news/inari-raises-over-200-million-to-unlock-the-full-potential-of-seed> Accessed 21-June 22.
  - 5 <https://www.businesswire.com/news/home/20200122005250/en/Ocuphire-Pharma-Announces-In-License-of-Phase-2-Oral-Small-Molecule-Drug-Candidate-for-Diabetic-Retinopathy-and-Diabetic-Macular-Edema-from-Apexian-Pharmaceuticals/> Accessed 21-June 25.

### INDIANA SEED FUND III

Indiana Seed Fund III ("ISF3"), BioCrossroads' currently active seed fund, is a \$9.0 million early-stage fund and was announced in 2018. ISF3 was formed to support a more vibrant capital environment and help ensure that there is a sufficient level of indigenous early-stage life sciences innovation capital in the State of Indiana. Like ISF2, ISF3 makes investments in early-stage biotechnology, pharmaceutical, medical device, diagnostic, ag-biotech and health information technology products and platforms and is a return-driven vehicle. Applying lessons learned from both the Indiana Future Fund and INext Fund programs, additional focus has been on cultivating relationships with fund managers investing in the region—leveraging our robust life sciences asset base, attracting additional investor attention and continuing to provide early support

and access to our most promising local life sciences start-ups.

Investors included BC Initiative, Inc., the for-profit arm of BioCrossroads, Eli Lilly and Company, Indiana University, Richard M. Fairbanks Foundation, Regenstrief Foundation, Walther Foundation, and the University of Notre Dame.<sup>24</sup>

ISF3 has completed investments in 10 companies to date which have raised more than \$210M in equity as of mid-2021 representing more than 23 times the investment made by the Fund in only three years.

On August 9, 2021, it was announced that Biolife Solutions (Nasdaq: BLFS) would be acquiring Sexton Biotechnologies in an all stock transaction valued at \$30 million

## Indiana Seed Fund III 2018



<sup>24</sup> <https://www.prnewswire.com/news-releases/biocrossroads-announces-the-formation-of-the-9-million-indiana-seed-fund-iii-invests-in-scioto-biosciences-and-animated-dynamics-300727668.html> Accessed 21-June 25.

providing a positive exit for the Fund less than two years following its investment in Sexton Biotechnologies and less than four years following its first investment. In the announcement, BioLife Solutions said that it plans to retain all Sexton team members and the current facility in the 16 Tech Innovation District in downtown Indianapolis. The transaction was closed on September 1, 2021.

In addition to returns to investors, the Fund has continued its strong partnerships with other early-stage life sciences sector investors including Elevate Ventures, University sponsored investment vehicles at Indiana University and Purdue University, and later stage investors including Frazier Healthcare Ventures, New Enterprise Associates, and OrbiMed.

### SEXTON BIOTECHNOLOGIES

In 2019, Sexton Biotechnologies was the first company incubated and spun out of Cook Regentec, a division of Cook Medical, located in Indianapolis. Production and operations are located at the 16 Tech Innovation District in downtown Indianapolis.

A team of about 20 people support Sexton Biotechnologies' products including bioproduction tools and media for cell and gene therapies. These products are currently embedded in more than 50 ongoing clinical trials.

Seed funding was provided by Cook, BioCrossroads, Biolife Solutions (Nasdaq: BLFS), and Casdin Capital. In September 2021, Biolife completed the acquisition of the Company in a stock transaction.<sup>1</sup>

1 <https://www.prnewswire.com/news-releases/biolife-solutions-closes-acquisition-of-sexton-biotechnologies-301367297.html>  
Accessed 21-September 7.

2 <https://www.biospace.com/article/releases/mbx-biosciences-closes-34-6-million-series-a-financing-in-rare-endocrine-diseases/> Accessed 21-June 25.

### MBX

MBX is the latest company formed to develop technology from the lab of Dr. Richard DiMarchi and is focused on developing therapies for endocrine diseases.

Repeat co-founders Dr. DiMarchi and Kent Hawryluk, were joined by co-founder Timothy Knickerbocker building Indiana's next generation of life sciences executive talent.

In less than two years, the Company attracted more than \$30 million in venture funding in a round led by Frazier Healthcare Ventures and joined by OrbiMed and New Enterprise Associates. BioCrossroads and IU also participated. Proceeds of the financing will support MBX as it advances its preclinical pipeline of peptide therapeutic candidates directed at clinically validated molecular targets.<sup>2</sup>

Indiana Seed Fund III Portfolio Companies <sup>25</sup>					
Name and Description	Type	Est.	Raised (millions)	Sold (millions)	Disposition
Sexton Biotechnologies, Developer of bioproduction tools for cell and gene therapy.	Life Sciences – Tools	2019	\$5.0	\$30	Acquired by BioLife Solutions (NASDAQ: BLFS) in August 2021.
Brickell Biotech, Developer of therapeutics for the treatment of skin diseases, including hyperhidrosis.	Life sciences – Therapeutic	2009	\$103.2	Operating/ Nasdaq: BBI	Clinical
Animated Dynamics, Developer of a biodynamic imaging platform intended to deliver drug assessment in three-dimensional living tissue samples.	Life sciences – Diagnostic	2013	\$8.9	Operating	Clinical
Gate Neurosciences, Developer of therapies for treatment of central nervous system disorders.	Life sciences – Therapeutic	2018	\$5.6	Operating	Clinical
Kovina Therapeutics, Developer of therapeutics to treat HPV-related cancers.	Life sciences – Therapeutic	2020	\$2M	Operating	Pre-clinical
Lumavate, Developer of low-code mobile application platform.	Life sciences – Technology	2015	\$9.3	Operating	Revenue
MBX Biosciences, Developer of therapeutics for treatment of endocrine diseases.	Life sciences – Therapeutic	2018	\$34.6	Operating	Pre-clinical
Novosteo, Developer of therapeutics for treatment of bone fractures.	Life sciences – Therapeutic	2017	\$6.4	Operating	Pre-clinical
Sabanto, Developer of farming-as-a-service technology using advanced autonomous equipment.	Life Sciences – Agriculture Technology	2018	\$5.0	Operating	Revenue
Scioto Biosciences, Developer of advanced bacterial therapeutics platform.	Life sciences – Therapeutic	2017	\$30.5	Operating	Clinical

<sup>25</sup> Information from portfolio companies from Pitchbook. Accessed 21-May 19.

## ECONOMIC IMPACTS OF FUND STRATEGIES

Investment funds like the Indiana Future Fund, the INext Fund, Indiana's Next Level Fund and BioCrossroads' Seed Funds are first and foremost designed as fiduciary investment vehicles to provide a financial return to their investors. Each investment made is evaluated on the ability to gain in value and return capital upon a sale or liquidation event, such as a public offering. Indiana's fund strategies were also designed to support and promote innovation, entrepreneurship, and a healthy economic ecosystem. Connecting venture capital to opportunities in Indiana activates a network of financial investors through syndicate partners. It is due to this practice, that the \$73 million Indiana Future Fund was

able to support 14 companies that raised \$631 million. These rounds of funding provide support for other positive economic impacts including job creation, sales generated from products developed by the investment, physical plant expansions, and ultimately wealth generated to fuel future investment activity upon a positive exit. These follow-on effects may not have been possible without the initial investment supported by the Fund of Funds and Seed Fund programs. Indiana has seen a tremendous amount of economic impact that would not have come to fruition without the design and execution of deliberate fund of fund and direct investment fund strategies, as illustrated by the table below.

Fund	Year Est.	Total Size (millions)	Funds Raised (millions)	Total Exits (millions), Other Impacts
IFF	2003	\$73	\$631	\$3,185+ (CoLucid, Endocyte), 50,000 SF mfg. center
INext	2008	\$58	\$105	\$362, 2020 sales for Emgality
Next Level	2017	\$50 <sup>26</sup>	\$435	Not disclosed, Inari @ 200 employees in W. Lafayette, IN
ISFI	2006	\$6	\$95	Not disclosed (SonarMed sold to Medtronic)
ISFII	2012	\$8	\$496	Not disclosed (Assembly Bio, Calibrium, MBX)
ISFIII	2018	\$9	\$210	\$30 (Sexton Biotechnologies)
Total		\$204	\$1,899 <sup>27</sup>	\$3,577+

<sup>26</sup> The Next Level Fund is a \$250 million fund of funds vehicle. Total Funds raised is listed for only those companies relating to life sciences including Inari and MBX. The amount of funds invested by the Next Level Fund in these companies is not disclosed but is believed to be less than \$50 million.

<sup>27</sup> Some companies were invested in by more than one fund, for example, SonarMed was invested by IFF and ISFI. Total funds raised controls for duplicate listings and therefore does not sum.



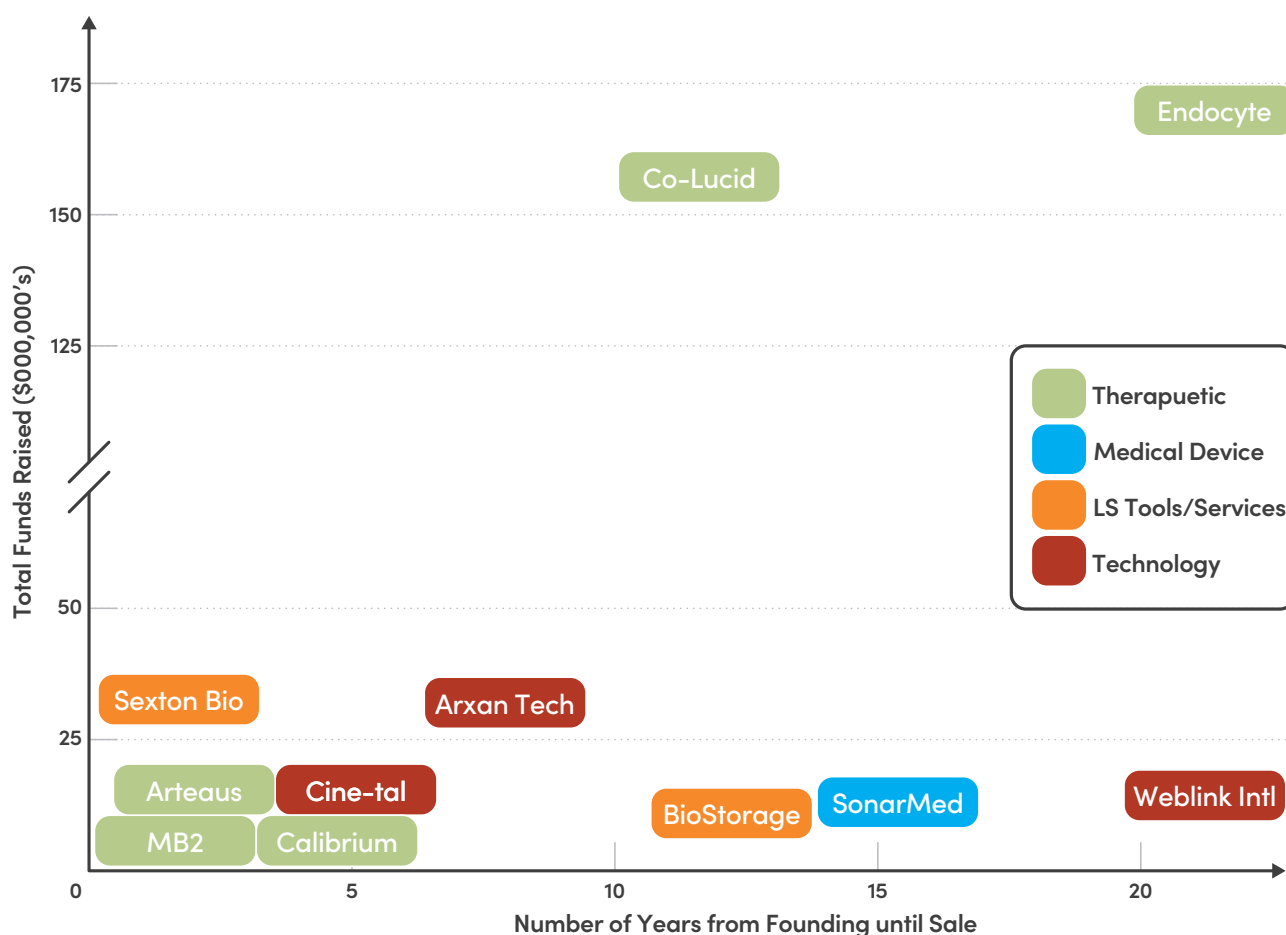
## PATTERNS OF SUCCESS

Eleven companies from the combined portfolios of IFF, INext, Next Level, and the BioCrossroads' managed seed funds have been sold through the date of this report. In the figure below, each of these companies is measured in terms of years from founding until sale on the horizontal axis and the amount of funding raised prior to sale on the vertical axis. In addition, they have been color coded to indicate whether they were developing a therapeutic, medical device, life sciences service, or general technology.

Of the 11 companies tracked, five were therapeutics and two were related to therapeutic development. Each of these were sold to major pharmaceutical companies or suppliers with Eli Lilly and Company purchasing Co-Lucid and Arteaus,

Novartis purchasing Endocyte, Novo Nordisk purchasing both MB2 and Calibrium, Brooks Automation purchasing BioStorage, and BioLife Solutions purchasing Sexton Biotechnologies. Interestingly, both Arteaus and Co-Lucid were originally licensed out from Eli Lilly and then repurchased following clinical trials.

While Arteaus, MB2 and Calibrium raised less than \$25 million in aggregate and were sold within three years of founding, both Co-Lucid and Endocyte raised more than \$150 million each to support multiple clinical trials and were sold after 12 years and \$2.1 billion after 23 years respectively. For therapeutic companies, the time from founding to sale averaged 10.3 years. MB2 was sold less than two years





from founding while Endocyte had about 23 years until its sale.

The sources of innovation were varied with four companies licensed from Indiana University or Purdue, four from life sciences companies, and three from other sources. Although listed as licensed from Roche following an acquisition of Marcadia, the technology developed by Calibrium originated from the laboratory of Richard DiMarchi at Indiana University. Conversely, Endocyte licensed PSMA-617 from ABX GmbH in October 2017 which catalyzed the sale of this intellectual property as well as one licensed from the laboratory of Philip Low at Purdue University in 1996.

As licensors of the intellectual property, both Indiana University and Purdue University received royalties as well as proceeds from sales of those companies. While each university has policies relating to intellectual property, most include a provision to

use some of the proceeds to support the originating lab as well as supporting the university at large. In addition to venture funds associated with the Indiana Future Fund and INext, local early-stage funds including Elevate Ventures, working hand in hand with Indiana Economic Development Corporation, and BioCrossroads' managed Seed Funds were investors in five of the companies namely Calibrium, Endocyte, MB2, Sexton Biotechnologies, and SonarMed.

Beyond the economic benefits, substantial impacts have been made and continue to be made from people and groups associated with these companies starting with building a base of talent growing in experience in raising funds, developing technology, and completing transactions which help bring new treatments and cures to patients. Both management and scientific talent associated with these successful exits continue to be active as entrepreneurs, innovators, and investors in Indiana's ecosystem.

University		Company	Other
Arteaus		Eli Lilly & Co.	
Arxan Technologies	Purdue University		
Biostorage			Start-up
Calibrium <sup>28</sup>		Roche <sup>1</sup>	
Cine-tal			Start-up
Co-Lucid		Eli Lilly & Co.	
Endocyte <sup>29</sup>	Purdue University <sup>30</sup>		
MB2	Indiana University		
Sexton Biotechnologies		Cook Regentec	
SonarMed	Purdue University		
Weblink Intl			Start-up

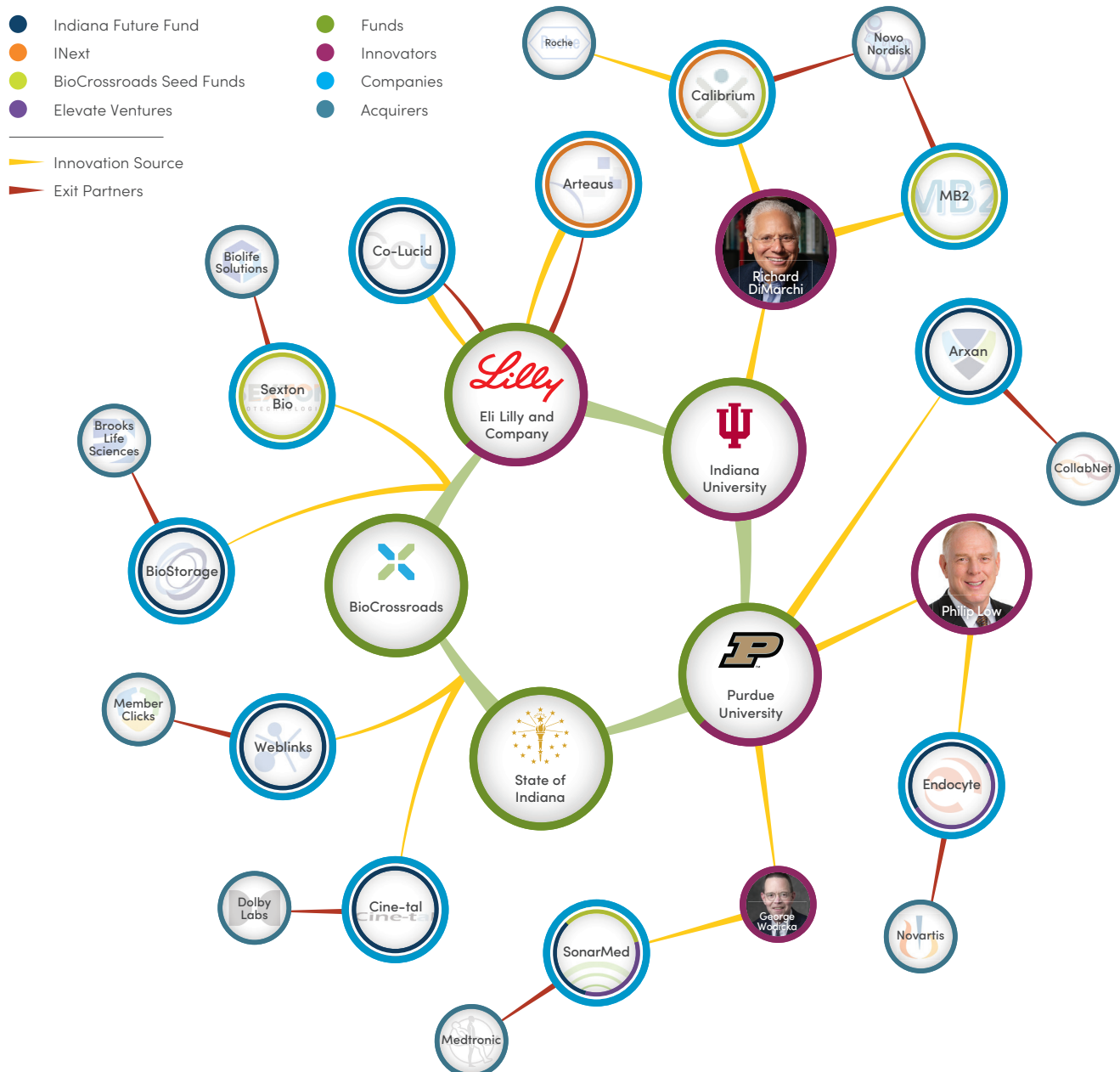
<sup>28</sup> Technology based on intellectual property originally licensed from the lab of Richard DiMarchi at IU to Marcadia and subsequently sold to Roche.

<sup>29</sup> Additional IP, PSMA-617, was licensed by Endocyte from ABX GmbH in October 2017. <https://www.globenewswire.com/news-release/2017/10/02/1138658/0/en/Endocyte-Announces-Exclusive-Worldwide-License-of-Phase-3-Ready-PSMA-Targeted-Radioligand-Therapy-for-Development-in-Prostate-Cancer.html> Accessed 21-June 25.

## INDIANA'S CATALYSTS

Mapping out these 11 successful exits to the sources of innovation, sources of funding and exit partners reveals a number of people and organizations that have served as catalysts namely are Indiana University, Purdue University, Eli Lilly and Company, the State of Indiana, and BioCrossroads. In the figure below, the

companies are marked with **cyan** circles along with a highlight indicating receipt of funding from Indiana Future Fund (**blue**), INext (**orange**), BioCrossroads Seed Funds (**green**), or Elevate Ventures (**purple**). The source of the innovation is shown through a **yellow** connecting line and exit partners are linked to target companies using a **red** connecting line.



### **Indiana University and Purdue University: Sources of Innovation and Capital**

Every great opportunity starts with an idea and universities are drivers of innovation. Indiana University and Purdue University are major research institutions with annual research expenditures in the hundreds of millions of dollars annually. Each has a function dedicated to supporting the transfer of this innovation to the marketplace through licenses or through company formation activities. In addition to providing the know-how necessary to secure the intellectual property, each also includes business advisory services to develop commercialization plans, and for some, early-stage investment funds to participate in early funding rounds. IU and Purdue each benefited from royalty and milestone payments from the companies sold as well as equity distributions for those companies where they also made direct investments.

For these 11 companies, five of the successful opportunities are the result of innovation from Indiana University or Purdue University. At Indiana University, Dr. Richard DiMarchi provided the innovation for both Calibrium and MB2. At Purdue University, innovation for Endocyte came from the laboratory of Dr. Philip Low; SonarMed from the laboratory of Dr. George Wodicka, including Dr. Jeff Mansfield and Dr. Eduardo Juan; and Arxan grew out of efforts by members of the Computer Science Department including Professor Mihail Atallah, graduate student Hoi Chang, Professor John Rice and Assistant Head Tim Korb.

Dr. DiMarchi and Dr. Low have demonstrated an outsized impact not only on those transactions listed above, but also on the overall innovation ecosystem.

**Richard DiMarchi – IU** A member of the National Academy of Medicine and the National Inventors Hall of Fame, his most important commercial contributions include molecular design of the first rDNA-derived peptide analog approved as a medicine, Humalog® insulin. He also contributed to the development of Forteo®, a peptide-based therapy for osteoporosis, as well as rGlucagon, and Humilin which annually sell in excess of \$5 billion.<sup>30</sup> Currently a distinguished professor at Indiana University, Dr. DiMarchi co-founded both Calibrium and MB2 which were sold in 2015 to Novo Nordisk. Following his extensive career at Eli Lilly and Company, he is also a founder of Ambrx, Marcadia, and MBX Biosciences. Merck, Roche and NovoNordisk are also independently advancing novel drug candidates inspired by discoveries of his laboratory at IU.<sup>31</sup> Dr. DiMarchi founded companies that have attracted funding from venture capital firms including 5AM Ventures, Frazier Healthcare Ventures, NEA, and Orbimed, among others. Ambrx currently trades on the New York Stock Exchange under AMAM, Marcadia was sold to Roche in 2010, and MBX Biosciences closed on a \$34.6 million raise in summer 2020. In addition, Dr. DiMarchi has served as a board member for many companies including Assembly Biosciences (Nasdaq: ASMB), Endocyte, and OnTarget Laboratories. A super connector, Dr. DiMarchi is a source of innovation, connector of talent, funder, and pathway leader for Indiana. He was recognized as the August Watanabe Life Sciences Champion in 2009.

**Philip Low – Purdue** A member of the National Academy of Inventors, Dr. Low has received many awards recognizing the impact of his discoveries in the treatment of cancer including the NIH MERIT Award, the Sosnovsky Award from the American Cancer Society, and the AACR Award for Outstanding

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<sup>30</sup> <https://www.invent.org/inductees/richard-dimarchi> Accessed 21-July 13.

<sup>31</sup> <https://archive.news.indiana.edu/releases/iu/2015/10/dimarchi-national-academy-of-medicine.shtml> Accessed 21-July 13.

Chemistry in Cancer Research, among others. Endocyte, founded in 1996, was sold to Novartis in 2018 and the company has plans to complete a 50,000 sq. ft. manufacturing facility in Indianapolis in 2023. Another company, OnTarget Labs, focused on illuminating cancer tumors for surgeons, is in Phase 3 clinical trials. Dr. Low's research is also focused on tissue regeneration, treatment of infectious diseases, reprogramming the immune system, and the treatment of erythrocyte diseases. Eight drugs stemming from his research are currently undergoing human clinical trials and seven companies, Endocyte, OnTarget Laboratories, Novosteo, Erythrocare, Inc., Umoja Biopharma, Morphimmune, and Eradivir have been founded to commercialize these discoveries.<sup>32</sup> These companies have attracted funding from venture capital firms including MPM Capital, DCVC Ventures, Casdin Capital, HIG Bioventures, and JJDC among others. Dr. Low is a prolific inventor whose innovations are providing substantial benefit not only to the treatment of disease, but also in providing opportunities for learning and growth of management talent connecting with necessary funding and impacting Indiana's innovation ecosystem. He was recognized as the August Watanabe Life Sciences Champion in 2013.

### **Eli Lilly and Company: Innovation, Talent and Capital**

Founded in 1876 by Colonel Eli Lilly, a pharmaceutical chemist and veteran of the American Civil War, Eli Lilly and Company ("Lilly") is central to the vitality of Indiana and the innovation ecosystem. Known as the inventor of insulin nearly 150 years ago, Lilly also was the first company to mass produce the Salk polio vaccine. More than 34,000 people are employed by Lilly throughout the world including about 11,000 at the headquarters in Indiana.<sup>33</sup> Annual economic impact from wages, R&D expenditures,

taxes, and indirect impacts from purchases are substantial. In addition, Lilly was an investor in the Indiana Future Fund, INext, and BioCrossroads' Seed Funds. Without Lilly as a Limited Partner, it is possible that none of these funds may have been established.

Lilly was not only the source of innovation for both Co-Lucid and Arteaus, but also the purchaser of these companies following completion of clinical trials. Marketed under the name Reyvow® in January 2020, the migraine therapy developed by Co-Lucid was approved in October 2019 as a new class of acute migraine treatment. The drug Emgality®, developed by Arteaus, was first approved in September 2018 for preventative treatment of migraine and in June 2019 for the treatment of episodic cluster headaches.

Indiana's management and scientific talent have also been developed at Lilly. Dr. DiMarchi was a senior research scientist at Lilly for 22 years. Many of those who have served as managers at companies formed to commercialize his technology also had experience at Lilly including: Jaswant Gidda, senior scientist who has also been associated with Marcadia, Anagin, and Gate Neurosciences; Fritz French, senior manager who was CEO of Marcadia, Calibrium, and board member at OnTarget Labs and Kovina Therapeutics; Mike Sherman senior manager who was CFO and then CEO of Endocyte for the license of PSMA-617 and sale to Novartis; Rob Brown, senior marketing manager and Dave McAvoy, senior legal, currently serving as CEO and General Counsel of Brickell Biotech; Derek Small, manager and Andy Dahlem, senior scientific leadership currently serving as co-founders, Chair and Chief Development Officer of Gate Neurosciences, and many, many others who are connecting with the early-mid- and later stage life sciences companies.

<sup>32</sup> <https://www.linkedin.com/in/philip-low-9a803a8> Accessed 21-July 13.

<sup>33</sup> <https://www.lilly.com/who-we-are/about-lilly/key-facts> Accessed 21-July 19.

### State of Indiana and BioCrossroads: Funders and Connectors

A discussion about catalyzing influences of these companies must also include the State of Indiana and BioCrossroads. Throughout this time, the State of Indiana has been supportive of innovation importantly through the establishment of the 21st Century Research and Technology Fund in 1999. Early on, most awards were granted to Indiana academic institutions to support early commercialization efforts, but many did not result in operating companies. In 2011, the State of Indiana pivoted to more directed economic development strategies which included expert advisory services and an investment model which more closely resembled venture investment. Through an arrangement with the Indiana Economic Development Corporation, Elevate Ventures was established and has invested in more than 427 companies throughout the State of Indiana including Endocyte and SonarMed.<sup>34</sup>

BioCrossroads participates as a connector and nexus for life sciences innovation serving as a guide to connect ideas and opportunity

with talent as well as an investor through its Seed Fund programs. Although it did not participate financially, it was the organizer of the Indiana Future Fund and INext serving on the Advisory Committee for both funds and connecting venture firms with Indiana opportunities. The Indiana Future Fund was a catalyst for the formation of Co-Lucid in 2012. INext provided an important role in Arteaus with Fund Participant, OrbiMed Ventures, providing funding alongside Atlas Ventures, co-founder of the company.

Beginning in 2005, BioCrossroads established the first of three seed funds allowing for direct investments in opportunities. During this period, BioCrossroads also worked closely with each of the universities as well as other area investors to build awareness and support the life sciences ecosystem. Often times as one of the earlier institutional investors, BioCrossroads completed more than 30 investments and has seen the maturation of the environment as the State and each of the universities have gone on to grow their early-stage investment strategies.

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<sup>34</sup> <https://www.elevateventures.com/about/> Accessed 21-July 13.



## FUND STRATEGIES – WHAT COMES NEXT

While the Indiana Future Fund and INext are long past their investment periods and realized significant returns, the Next Level Fund and each of the Indiana Seed Funds managed by BioCrossroads have active portfolios. Indeed, both the Next Level Fund and Indiana Seed Fund III are still within their investment period. The necessity and impact of these capital strategies is apparent. The presence of active and engaged capital helps assure that Indiana innovation can be developed here, and as seen with Novartis's development of a manufacturing facility for the Endocyte asset, the approvals of Emgality® from Arteaus, and Reyvow® from Co-lucid, directly adds to the economic base as innovation is commercialized.

The current version of Indiana's Fund of Funds strategy, the Next Level Fund, is not dedicated to life sciences, but also includes technology funds. To date, three of the 14 funds invested -- Acre, 5AM and Frazier Healthcare Partners -- invest in life sciences and two companies have received investment: Inari and MBX. It will be important that more life sciences funds participate in the program to support the innovation coming from our research universities and from our corporate sector. Created by the Indiana General Assembly in 2017, this Fund is focused on supporting economic activity in Indiana to attract, assist, and retain quality technology businesses in Indiana. As one of the nation's leading centers for life sciences, and as the second largest exporter of life sciences products, it is clear that life sciences are a vital and necessary part of Indiana's economy.

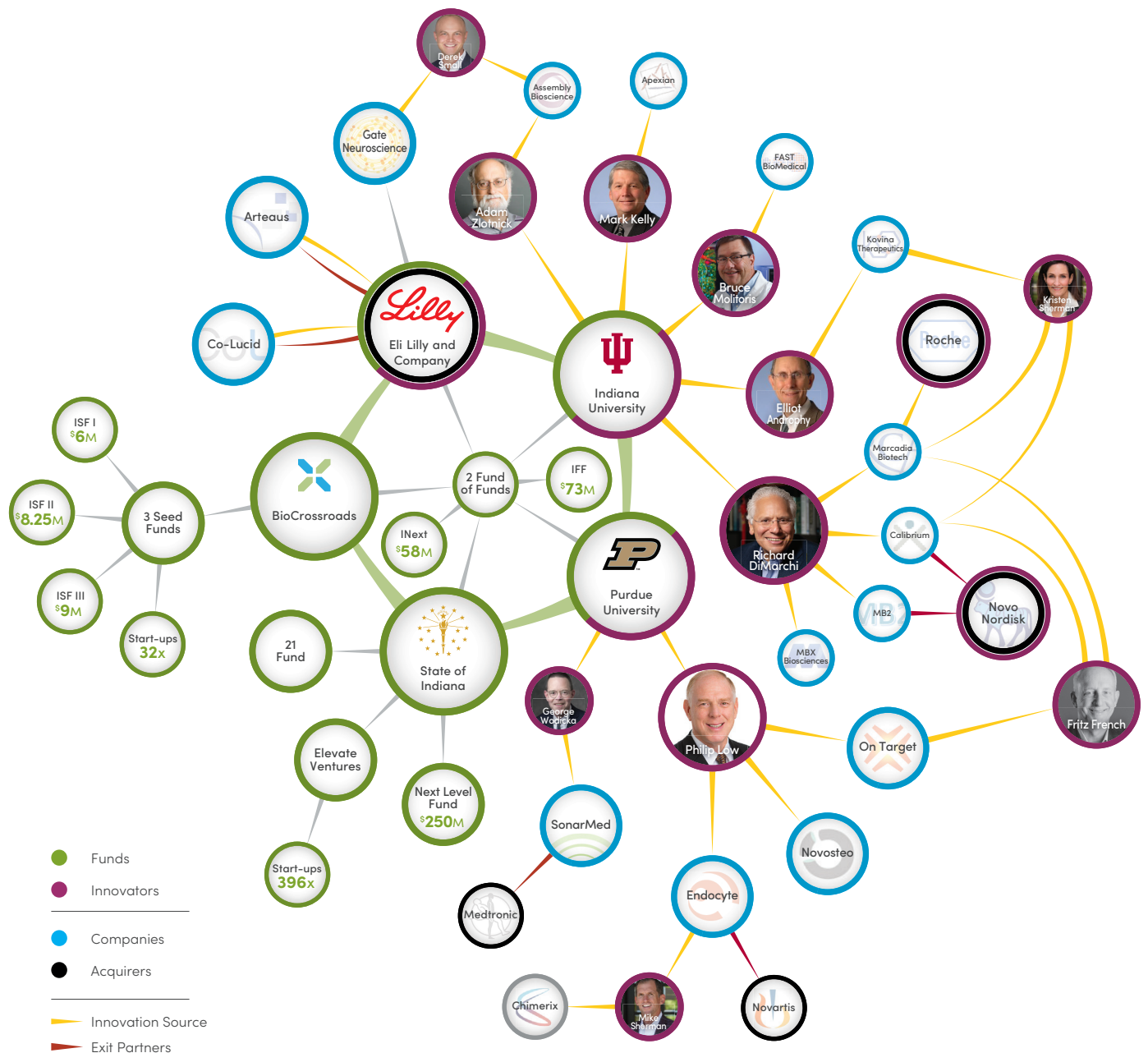
Early-stage seed funding is a fundamental part of any innovation strategy. The continued support of the successful

Elevate Ventures strategy must continue. As Indiana's most active Venture Capital Investor, Elevate has invested nearly \$120 million to date in 427 companies in 87 counties across the state. Joining Elevate are Indiana's research universities, each with early-stage seed fund programs. IU's seed fund programs through the Innovation and Commercialization Office, has made critical early-stage investment in technology developed at Indiana or by Indiana alumni using funds through its IUPhV investment fund or through coordinating Angel investment funds. Purdue University has a number of programs and at least four funds administered through the Purdue Research Foundation including the Trask Innovation Fund, the Ag-celerator Fund, Purdue Start Up Fund, and the Foundry Investment Fund. In the last five years, Purdue has launched more than 100 companies. The University of Notre Dame also has its Pit Road Fund to support innovation from the university. The fund is also augmented by a number of programs, including the IDEA Center's McCloskey New Venture Competition which provides upwards of \$400,000 in prizes annually. All of these programs help ensure that innovation generated from universities are supported and encouraged to be commercialized.

BioCrossroads continues to play an important role. At the nexus of Indiana's life sciences ecosystem, BioCrossroads is where Indiana's life sciences stakeholders focus on the collective. It has ignited Indiana's life sciences capital strategy beginning with the first Fund of Fund vehicles and serving as a trailblazer in supporting promising companies with seed funding, often as one of the first institutional investors. Not only as an investor, BioCrossroads has amplified and extended the efforts of other catalysts

in driving innovation supporting Elevate's annual Kinetic conference, raising awareness and supporting tech transfer efforts at each of IU, Purdue, and Notre Dame, supporting the AXIS program to provide mentoring from experienced managers to early-stage company CEOs, and many more activities in addition to making direct investments.

These activities have helped support the growth of the map from those 11 companies, which have already met with success, to preview many more that may be successful over the next decade. In the figure below we see the generational impact that has resulted from Indiana's collective experience and investment in innovation. We're excited about what comes next!





1210 Waterway Blvd., Suite 5000  
Indianapolis, IN 46202  
317-238-2450

[www.biocrossroads.com](http://www.biocrossroads.com) | [www.biointellex.com](http://www.biointellex.com)