MAP Team 171

University of Michigan
Center for Discovery of New Medicines

Final Report

April 29, 2015

A Strategic Plan for the Center for Discovery of New Medicines

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EXECUTIVE SUMMARY

The drug discovery landscape is complex, evolving, and increasingly requires the innovation of academia. Opportunities for translational research have expanded as academic drug discovery centers (ADDCs) proliferate, biopharma externalizes innovation in its pipeline, and venture capitalists shift funding to preclinical projects. For the Center for the Discovery of New Medicines (CDNM) to guide the drug discovery community at the University of Michigan, bridge gaps between principal investigators and industry, and become a leader among ADDCs, we propose the following recommendations:

PROGRAM STRUCTURE

Project Selection

Establish a diverse scientific advisory board (SAB), made up of representatives from industry, startups, clinicians, researchers, and intellectual property (IP) experts, to best guide which proposals should be awarded with funding.

Navigation

Appoint research navigators to guide PIs throughout the drug discovery process by identifying and coordinating resources to move projects forward, monitor adherence to the project plan and milestones (or adjust plans as necessary), and smooth collaborations between PIs and core lab directors during the course of a project.

Alliances

Appoint an industry alliance manager to connect promising projects to private sector partners, increase the center's profile in industry and VC business development circles, and build relationships between the private sector and CDNM.

EDUCATION

Curriculum Development

Develop a creative drug discovery curriculum with interactive educational opportunities that considers the interests and priorities of the faculty, postdocs/PhDs, and staff at UM. CDNM will have a higher chance to develop programming that will garner campus support by including internal stakeholders in curriculum creation.

CDNM Grantees

Establish a required, bi-weekly education curriculum for project team members who receive CDNM grants, which includes technical guidance for each stage of the project, as well as a variety of co-learning opportunities, where teams would update one another on their latest project status. Based on primary research, we have found that educational programming, along with a supportive community for translational researchers, is key for project success.

Post-Docs and PhDs

Engender a sense of community for postdocs and PhDs by soliciting programming ideas (i.e., mentoring opportunities, networking events with industry, and professional development retreats/dinners) from them.

OPERATIONAL STRUCTURE

Support Core Consultations

Support 10-20% of the core labs' costs to cover lab leader consultations on drug discovery projects. CDNM has a strong core foundation, but core lab leaders spend a lot of time consulting and advising on projects without compensation.

Motivate PI Participation

Shift how CDNM funding is disbursed to grantees. Rather than funding through recharge, CDNM should dole out funding to PIs through reimbursement. This shift will help mitigate funding gaps for supplies and resources PIs need for their labs during the course of the project.

SUCCESS METRICS

Shared Metrics (CDNM, Industry, VCs) Leveraged by all Stakeholders

The two major metrics shared across all stakeholders would be number of publications generated from CDNM supported projects and IP (Patent) Licenses.

Internal (CDNM) Metrics

Additional internal metrics that CDNM should consider include, number and amount ($) of follow-on grants generated, collaborations generated from CDNM support, and projects supported by CDNM.

BRANDING

CDNM should reinvent its' internal brand, and establish its own identity, by being rebranded as "University of Michigan Drug Discovery" (UMD^2). In addition, there should be a clear distinction between UMD^2 and LSI, starting with its URL.

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INTRODUCTION

Biopharma innovation is a lengthy, capital intensive, and risky process. Drug discovery and development typically takes 15-20 years, but can take upwards of 40 years, in some cases.[1] A new drug can cost anywhere from $1-2 billion to bring to market.[2] As a result, drug discovery and development projects require a broad range of stakeholders, including (but not limited to) academic institutions, basic science researchers, applied science researchers, clinicians, intellectual property lawyers, venture capitalists, and biopharma.

The drug discovery landscape changes at a rapid pace, as companies race to develop the next novel medical offering. Over the past several years, the biopharma industry has benefitted from a strong macroeconomic environment that has fueled industry consolidation and M&A activity.[3] However, biopharma companies are increasingly offloading the risk in their R&D portfolios. From 2010 – 2013, 64% of late-stage pipeline valuation for biopharma companies came from external sources, including acquisitions, joint venture and co-development strategies and licensing.[4] As a result, biopharma companies have continued to lay off employees in R&D.[5]

Simultaneously, academia is facing plateaued funding for basic research from NIH,[6] as priorities are shifting towards translational research.[7,8,9] As industry continues to externalize its early stage R&D activities, academic institutions, like UM, should contribute to the biopharma innovation gap in order to expand its funding sources, while also fulfilling the academic mandate to progress scientific knowledge and positively impact the world.

While the goals of pharma and academia are not fully aligned, the potential for shared benefits cannot be overlooked. Biopharma companies are eager to collaborate with academia to support drug discovery efforts. In turn, industry can support academia in expanding its research activities. While some academics may be skeptical of collaborating with industry, others believe academics have an obligation to support the advancement of science through drug discovery. When academic institutions open themselves to collaborating with industry partners, academics can mitigate the decline of government research funding, increase collaborative science, and fulfill their moral obligation by supporting drug discovery efforts with biopharma to improve global health outcomes.

PROJECT SCOPE

The Center for Discovery of New Medicines (CDNM), founded in 2012, facilitates drug discovery at the University of Michigan (UM). CDNM offers a support system and resources to advance small molecule therapeutic projects from target validation to clinical proof-of-concept. CDNM supports primary investigators (PIs) at UM by providing seed funding (up to $50,000) to be used in the UM core labs (High-Throughput Screening, Structural Biology, Medicinal Chemistry, and Pharmacokinetics). Additionally, CDNM provides project-specific mentoring and consultation from industry-experienced experts to advance projects to the next stage of the drug discovery process.[10]

As part of the MBA core curriculum at UM Ross School of Business, MBA students engage in a Multi-Disciplinary Action Project (MAP). Students work in teams to tackle a real-world problem currently faced by an organization, while applying the principles and skills learned during their first year core courses. The 2015 MAP team for CDNM is comprised of four members (see Appendix A for biographies).

The 2015 MAP team was enlisted to develop a strategic plan that will position CDNM as a leader in academic drug discovery. The team conducted a landscape assessment of academic drug discovery, identified challenges and opportunities for financial sustainability, and developed a data-driven, strategic plan that enables CDNM to improve drug discovery at UM. The project scope focused on the following:

- Explore the current drug discovery landscape by benchmarking CDNM against other academic drug discovery centers (ADDCs) and identifying opportunities for industry partnership
- Evaluate the current financial and operational structure for CDNM; provide recommendations for reaching financial and operational sustainability
- Evaluate the perception of drug discovery at University of Michigan among Principal Investigators (PIs) and assess the brand equity of CDNM
- Provide an educational strategy to incite behavior change and interest towards drug discovery among PIs at University of Michigan

RESEARCH METHODOLOGY

The project plan and timeline was reviewed with and agreed upon by the Director of CDNM and the MAP team (see Appendix B for detailed plan and timeline):

Phase 1: Engagement Definition and Preliminary Research (March 9-20)
Phase 2: Data Collection at University of Michigan (March 23 – April 2)
Phase 3: External Data Collection (April 6 - 17)
Phase 4: Project Wrap Up (April 20 – 29)

Secondary Research Methodology

The team conducted secondary research throughout the project to better understand the various stakeholders' landscapes (government agencies, academia, venture capitalists/VCs, and industry partners), current models of academic drug discovery centers, industry and academic partnerships, and the financial implications of the drug discovery process. To do so, the team utilized internet resources (e.g., Wall Street Journal, Fierce Biotech/Pharma, NPR, etc.), industry reports (e.g., Analysis Group, PhRMA, EvaluatePharma, Deloitte, etc.), and scientific literature (e.g., Nature, Science, Drug Discovery Today, etc.).

Primary Research Methodology

The team conducted primary research to gather direct insights and perspectives from various stakeholders within the drug discovery and development industry. The team created interview guides iteratively and customized questions for each stakeholder (i.e., academic, biopharma, or VCs). An interview guide example can be found in Appendix C.

The interviews primarily took place face-to-face in Ann Arbor, Cambridge/Boston, and San Francisco/Bay Area, although some were conducted via phone. The interviews were conducted with all four team members, and notes were compared and confirmed post-interview to ensure data quality. Over the course of the project, the team performed 50 interviews, covering academia (31), industry representatives (12), and VCs (7). A more thorough breakdown of interviewees and their association can be found in Appendix D.

To understand the landscape of academic drug discovery centers (ADDC) in the US, the team administered a survey sent to a list of all US ADDCs (84 in total, as of April 2015) and their contact information from the Academic Drug Discovery Consortium website.[11] Working with the Director of CDNM, the team formulated a survey in Qualtrics, which was vetted by the Communications Manager at the Ross School of Business for proper survey design. The survey was distributed to all ADDC members on behalf of the Ross MAP students and CDNM, and responses were collected over three-weeks. A detailed list of the survey questions can be found in Appendix E.

Finally, the team conducted an internal survey to UM PIs. The team created a list of life sciences PIs (811 in total, as of April 2015) using the UM directory (MCommunity)[12]. Through the survey, the team aimed to gauge interest of UM PIs in translational research, identify what resources they utilize for drug discovery projects, and inquire how they feel the emphasis on translational research will change in academia going forward. The survey was distributed to the UM PIs on behalf of the Ross MAP students and CDNM, and responses were collected over a two week period. A detailed version of the survey can be found in Appendix F.

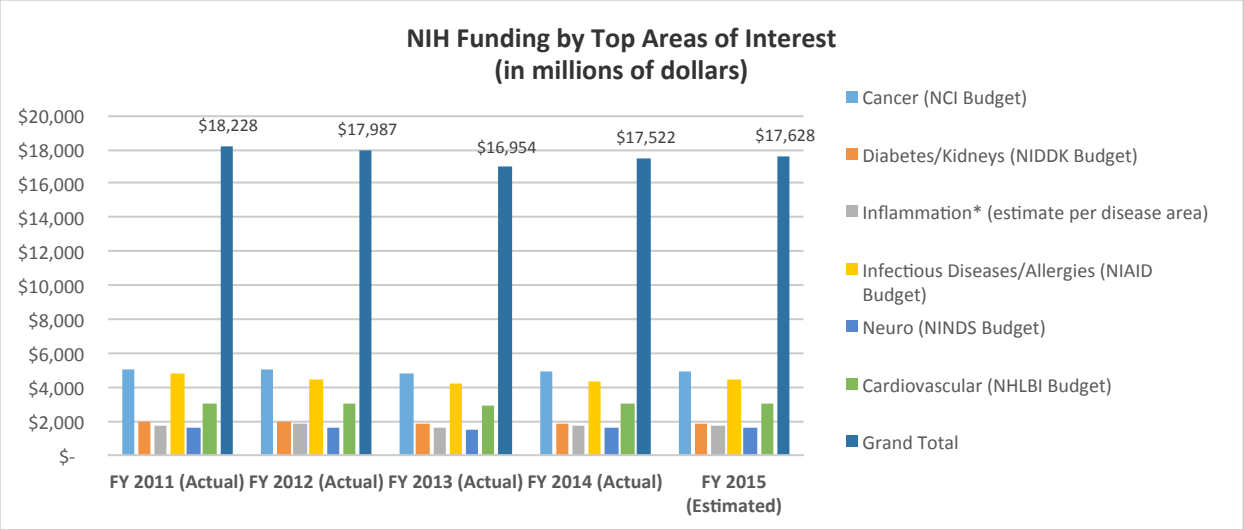
OBJECTIVES

Overall, the team aimed to create a strategic plan for CDNM that was well informed by the current drug discovery landscape and the appetite and resources available for drug discovery at UM. Using this foundation, the team would develop an optimal program strategy and structure for CDNM to ensure that the center could evolve into an effective and efficient ADDC. Moreover, the team would recommend ideas for how CDNM could better educate and engage the UM life sciences community in drug discovery. Additionally, the team would deliver a funding strategy to ensure CDNM can sustainably fulfill its mission. Finally, the team would establish success metrics to allow CDNM to track its progress and impact in drug discovery.

DRUG DISCOVERY OVERVIEW AND TRENDS

Given the current volatile and dynamic state of drug discovery, with biopharma companies facing increased competition from other large companies as well as smaller market entrants (i.e. biotechs), many have taken advantage of the strength of the economic environment via mergers, acquisitions, or asset swaps to stay ahead of the competition.[13] At the same time, academia is increasingly struggling to gain access to NIH funding for their research programs[14] (see **Figure 1** for CDNM's disease areas funding trend), leading to the increased interaction between biopharma and academic institutions.

Figure 1. NIH Funding by Top CDNM Interest Area[15,16,17,18,19,20]



To better understand how these alliances manifested, the team analyzed the competitive landscape by assessing the strengths and weaknesses of the biopharma's R&D value chain:

- **Minimal threat of new entrants**: At the macro level, no companies could realistically enter as a diversified biopharma company, due to the time and capital intensive nature of R&D operations. Yet on a disease by disease basis, small biotechs could enter the market posing competition to the existing players (e.g., Cubist), sparking M&A activity.
- **Increased dependence external R&D suppliers**: Biotechs, Academia, and CROs can be seen as suppliers. Given today's macroeconomic environment, biopharma is relying on these entities more heavily as they shift from fixed to variable R&D costs.
- **Priority on first to market**: With increased competition among end customers (payers, providers, and consumers), they have become increasingly price sensitive. Biopharma companies strive to become first to market and offer a product that not only improves health outcomes, but also makes sense economically, in order to meet customer demands.
- **Growing consolidation**: Biopharma companies compete fiercely to sustain profitable drug pipelines. Over the past 15 years, fifteen multi-billion dollar biopharma firms have consolidated to 20, illustrating the need to dominate market segments.

Taking into account the competitive landscape for biopharma R&D, CDNM (as well as other ADDCs) can position themselves within the drug discovery environment to become a reliable supplier of biopharma R&D innovation.

BIOPHARMA INDUSTRY

TRENDS

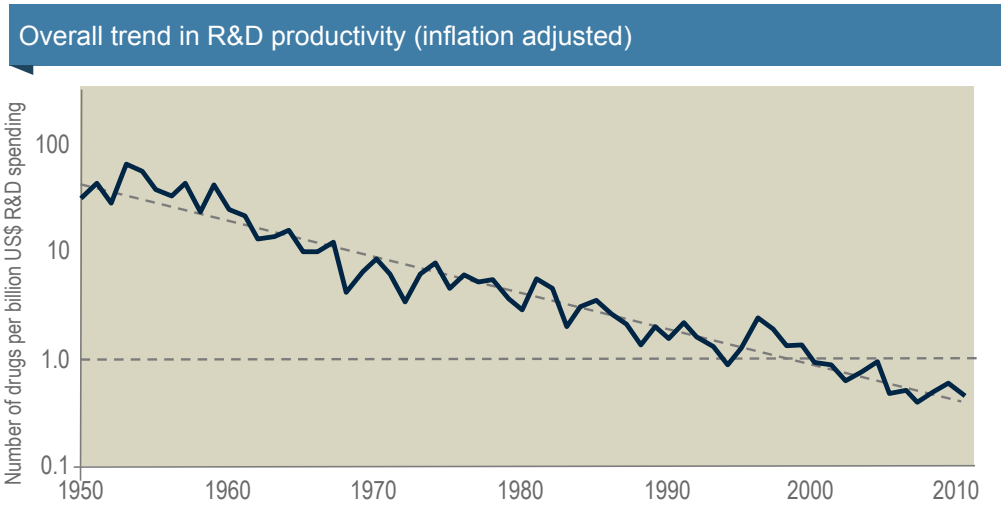
Biopharma companies have faced a difficult market climate since the 2008 financial crisis. In the constrained capital environment, biopharma companies have shifted their R&D

strategies to de-risk their portfolios. While the biopharma sector has been rapidly rebounding in the past couple years, companies have preserved their conservative outlook on biopharma innovation. As a result, biopharma companies are shifting their approach to collaborating with academic institutions. Key trends in driving these behaviors include:

- the decline in biopharma R&D productivity
- the increase in clinical trial failure rates
- a shift from fixed to variable cost structures via outsourcing and alliances
- increase in access to capital (due to favorable macroeconomic conditions), and reduction in risk exposure
- the stringent regulatory environment
- the evolving reimbursement environment from employer-based to individual

Biopharma companies are experiencing a decline in R&D productivity. In a study by Jack W. Scannell et al., R&D productivity[i] has declined significantly since 1950 (see **Figure 2**)[21]. According to the study, the number of FDA approved new drugs per billion R&D dollars spent has been halved approximately every 9 years.

Figure 2. Marked decline in R&D productivity



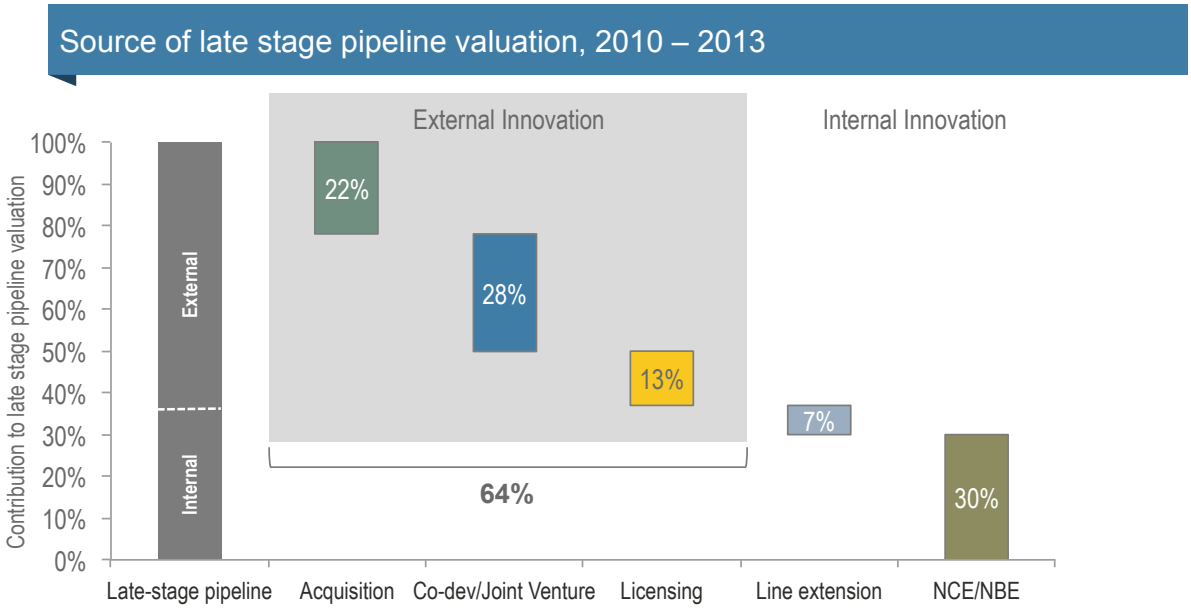
R&D productivity has declined largely because of high failure rates, particularly during in-human clinical trials. From 2003-2011, a new drug had a 10.4% likelihood of approval (LOA)[22], compared to 16.0% from 1993-2004.[23]

The R&D productivity decline has pressured biopharma companies to outsource R&D activities to reduce fixed costs and improve productivity. As mentioned earlier, 64% of biopharma late stage pipeline has been sourced from external sources (see **Figure 3**), illustrating biopharma's reliance on outside innovation.[24] According to a report by Accenture, biopharma companies are increasingly using specialty niche providers, or

[i] R&D productivity is defined by the number of new drugs per $US billion R&D spending per annum. R&D spending is based on US government estimate and PhRMA annual survey 2011.

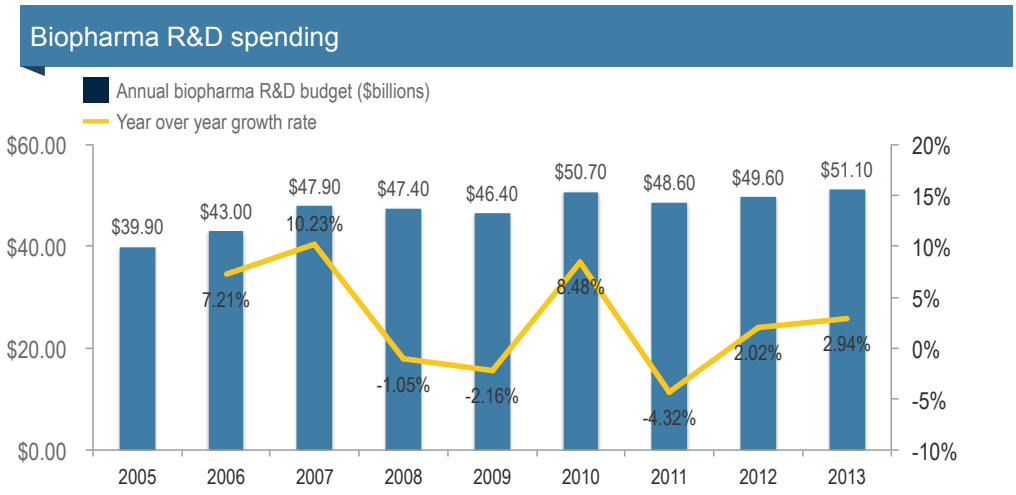
contract research organizations (CROs), in order to shift towards a more variable cost structure.[25] Academic institutions have risen as promising partners for outsourcing biopharma innovation, particularly as it relates to target identification and validation.

Figure 3. Source of late stage pipeline valuation, 2010-13



According to PhRMA 2014 Profile, R&D spending of biopharma has been steadily growing since 2009 (see **Figure 4**).[26] Ernst & Young pointed out in their report that the amount of capital made available by investors helped fuel the rebound in R&D spending.[27] Increasing amount of capital made it easier for biopharma companies to partnership with academics to accelerate drug discovery.

Figure 4. R&D spending from 2006 to 2013[ii]



[ii] Biotech R&D spending data is from E&Y Beyond Borders Global Biotechnology Report 2008-2014. Where annual reports provided inconsistent R&D spending data, data from latest report were used. Some companies included in both cohorts.

The biopharma industry is known for being highly regulated. Even after clinical trials, a new molecular entity (NME) can take a long time to be approved. From 2009-2012, half of NME applications were approved on their first submission. In turn, 96% of NME applications were approved after being resubmitted.[28] Even once approved, the FDA may instate post-marketing requirements and commitments (PMCs), which may require additional clinical trials, and thereby increase costs. PMCs have sharply increased from 58% (2004-2006) to 88% (2010-2012).[29]

With regard to the reimbursement environment, the biopharma industry is facing increased pressure from health insurers to justify drug prices. In particular, the Affordable Care Act is placing a higher burden-of-proof for biopharma companies to demonstrate both economic and clinical value of a new medicine.[30] As a result, biopharma is less incentivized to pursue drugs that only offer an incremental improvement to human health.

In response to the shifting macro environment, biopharma companies are relying on academia as a key source for innovation – particularly on academic researchers who have deep expertise in target identification and validation. That said, biopharma companies are reconsidering how to interface with academia. Historically, biopharma companies established academic research partnerships with unrestricted funding. However, biopharma companies have realized that these unrestricted funding agreements have not yielded a meaningful return on investment. As such, biopharmas are engaging with academia on targeted projects with specific milestones and metrics.

For example, Pfizer used to provide multi-year, institutional level, unrestricted funding to academia. One example included a $20M partnership with Scripps Research Institute. However, these partnerships can no longer be supported, and have been reduced significantly. Instead, Pfizer is focusing on specific projects related to therapeutic areas listed on its R&D partnering brochure.

Pfizer is not the only biopharma company pursuing these targeted partnerships, as several biopharmas are experimenting with new types of academic partnerships.

APPROACH

Biopharma companies rely on academia to add value to drug discovery through novel target and biological pathway identification. Through interviews, the team learned that biopharmas are willing to engage in partnerships with academia at varying discovery phases, as long as it is synergistic with their portfolio strategy. How biopharma engages with academia depends on the drug discovery phase.

Pre-Target Identification

Biopharma companies are interested in collaborating with academia during the pre-target identification stage because academia can contribute a deep understanding of the biological pathway that can be used to find novel targets. Biopharma companies have strong expertise in chemistry, but acknowledge their struggles with target identification. For example, the Broad Institute is an ADDC that collaborates with multiple biopharma

companies on target identification. Because of the Broad's expertise in genetics, biopharma companies are eager to forge these relationships. In order to expand early discovery collaborations, biopharma companies have established several experimental partnerships with academia in recent years.

One example is the trend of biopharma companies establishing regional collaboration hubs to promote early drug discovery. In 2011, Pfizer established four Centers for Therapeutic Innovation (CTI) in Boston, New York, San Francisco, and San Diego to encourage real-time collaboration between academic and Pfizer scientists on drug discovery and development projects for unmet medical needs. Each CTI, which accepts project proposals from faculty in nearby universities, hosts 20 academic scientists and 20 Pfizer scientists. If selected, Pfizer will provide the faculty with funding to support a postdoc to work on the project at the CTI half of his or her time. Pfizer may provide additional funding when predetermined milestones are met. CTI research exclusively focuses on biologics.

In 2012, Merck collaborated to create the California Institute for Biomedical Research (Calibr), an independent, not-for-profit research institute dedicated to advancing basic biomedical translation. Calibr looks to hire high profile faculty to conduct its research. Merck will fund Calibr with up to $90 million over seven years, with an option to obtain exclusive commercial licenses from work Calibr's work.

Johnson & Johnson has also established Innovation Centers in Boston, California, London, and Shanghai to facilitate business development, while also providing consultation to academic researchers. These Innovation Centers have veteran R&D and product development leaders, experienced investors, legal advisors and business development professionals to support early to proof-of-concepts stages.

In addition to regional collaboration hubs, the team learned that some biopharma companies have established joint steering committees for academic drug discovery programs. In 2010, Sanofi launched the MIT-Sanofi Biomedical Innovation Award Program. Sanofi established this program to broaden its relationship with MIT from a single lab focus to an institutional level. In order to manage the alliance successfully, Sanofi established a joint steering committee with 4 MIT faculty and 4 Sanofi executives to select drug discovery projects. In addition, Sanofi has employed a full time staff member to manage project progression. Through this award program, Sanofi has funded 14 projects, resulting in 2 projects being brought in house and 1 spinoff. Sanofi has made similar strategic alliances with Caltech, and is now looking to expand this program to 10 more universities.

Target Identification to Hit

While academics are effective in identifying novel targets and assays, academic screening compound libraries are often not sufficiently robust or proprietary to find viable hits for drug discovery. To bridge this gap, some biopharmas have opened their screening libraries to collaborate with academia in identifying viable hits (see **Figure 5**).

Figure 5: Drug discovery process -- Biopharma engages pre-hit

Typically, these screening opportunities are available for all research scientists. Further, should the scientist yield a promising hit, the partnering biopharma company will likely seek further collaboration with the academic.

In 2009, Lilly launched Open Innovation Drug Discovery Program (OIDD), an online platform for researchers to submit small molecules for drug screening. Through OIDD, Lilly provides access to internal screening assay modules and publication quality biological data to test hypotheses, which could lead to collaboration with Lilly to bring discovery of novel therapeutics forward. OIDD ensures the investigator retains IP rights to the molecule by creating a secure environment to transfer information between Lilly and the investigator through a web-based application.

GSK also launched the Discovery Fast Track Challenge in 2013, which provides winners of the challenge with access to GSK's HTS chemical library comprised of approximately 2 million compounds. If the result is promising, and both GSK and the institution wish continue collaborating, further research funding could be provided.

Such open innovation models can be considered as low-cost model to facilitate collaborations between academia and industry, with the potential of further research funding toward developing new medicines.

Hit to Clinical Candidate – Traditional Licensing Deals

Biopharma companies can begin licensing discussions as early as hit identification (see **Figure 6**), a strategy mentioned by several biopharma executives in the team's interviews. However, through conversations with ADDCs, the team confirmed that there are no documented cases where biopharma companies have engaged with academic institutions pre-hit. Although biopharma companies look for novel targets from academia, a target does not generate significant value or intellectual property, but rather the chemical structure. This likely explains why biopharma companies, in practice, do not engage pre-hit. Once a promising chemical structure is identified, biopharma companies can use its strength in medicinal chemistry to quickly advance the drug discovery process.

Figure 6: Drug discovery process -- Biopharama licenses post-hit

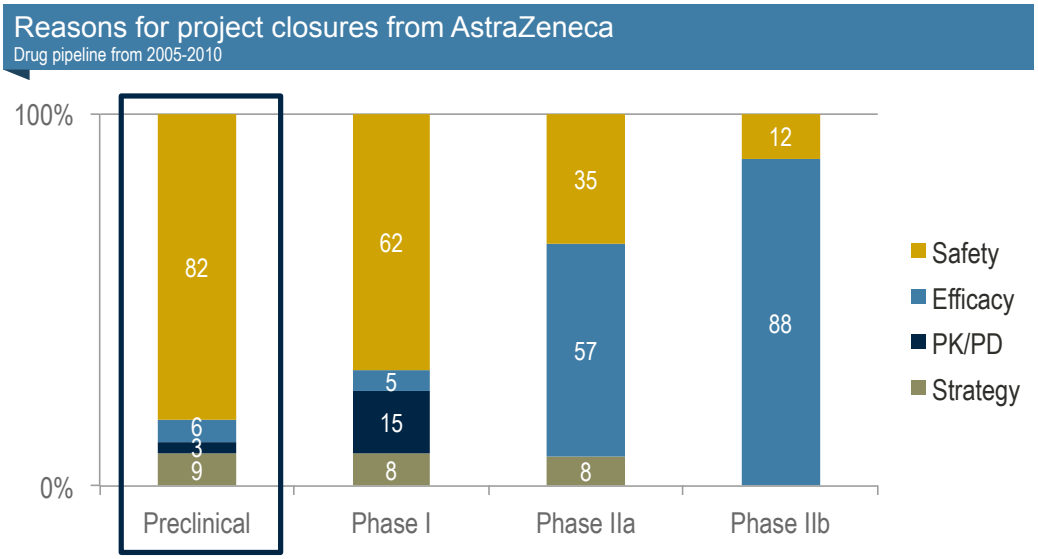
Business development units in biopharma primarily rely on publications to become aware of prospective projects. In turn, biopharma business development will engage their internal scientists to gauge whether the finding is sufficiently novel and worth pursuing.

In addition to publications, personal relationships were frequently mentioned as a critical role in developing industry-academic partnerships. For example, June Lee, Director of the Early Translational Research (ETR) Program at University of California – San Francisco (UCSF), explained that the ETR Program has received industry funding as a result of her personal networks. Similarly, alliance representatives from both Biogen and Pfizer mentioned that academic partnerships are primarily established via personal connections.

Biopharma does not rely on technology transfer offices to identify prospective deals, as they typically do not have salient information about the value of ongoing research projects. For example, tech transfer offices typically offer 1-2 page disclosures of inventions, yet these documents rarely contain relevant information for biopharmas identify promising projects. Furthermore, tech transfer office staff typically do not have deep expertise in therapeutic areas, nor do they have sufficient bandwidth to continuously engage with biopharma about high value projects.

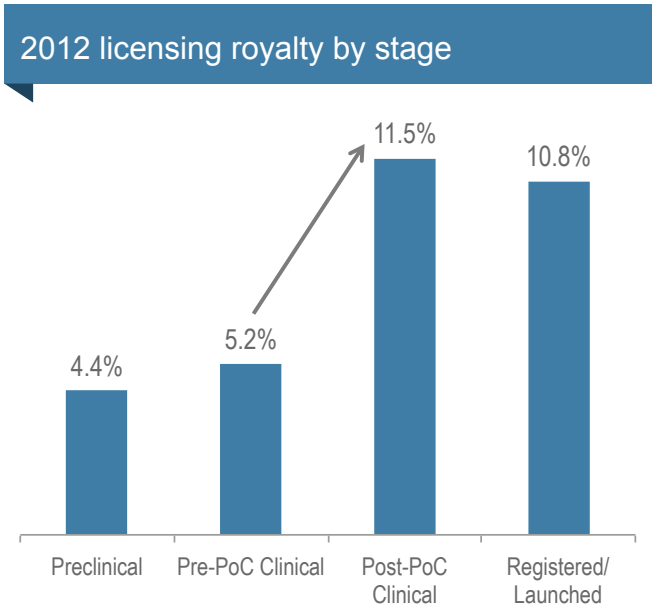
Once biopharma identifies a potential deal, type of data sought out in following through with the deal was not made clear. Presumably, biopharma companies perceive this information to be their "secret sauce," explaining the reluctance to disclose the details. However, the team learned of a few considerations when compiling a data package for a project. First, toxicity and efficacy are often the primary concerns for biopharma companies. For most diseases, high toxicities and poor efficacy will kill a project internally. According to a David Cook et al. study on active AstraZeneca projects from 2005-2010 (see **Figure 7**), 82% of preclinical and 62% of Phase 1 project closures were attributed to safety. More than 57% of Phase 2 project closures were attributed to efficacy[31].

Figure 7. Reason of project closure for AstraZeneca during 2005-2010



Biopharmas also look to see Proof-of-Concept (POC), though exact specifications for this were undefined. According to a survey from the Licensing Executives Society, universities earned 6.3% more royalty payments once POC was establishes (see **Figure 8**).[32]

Figure 8. Average royalty of deals in 2009 and 2012



From our interviews, biopharma frequently mentioned the difficulties working with academics, as they have a poor understanding of drug discovery process. One cause of this is that academics underestimate the data quality necessary for biopharma companies to advance drug discovery projects, as it is much higher than what is required for publications. In addition, academics are often unaware of the desired animal model to use for drug discovery. Therefore, it would be greatly beneficial for academics to have a research navigator with industry experience to guide PIs through the complicated drug discovery process.

Typically, academics do not fully grasp what drives industry interest (i.e., findings that support unmet medical needs, having commercial viability, being first/second to market, or clearly proven superior clinical benefits). Moreover, tech transfer offices do not understand how to market novel ideas, and are not effective in providing relevant data to attract biopharma interest. Therefore, it is important for ADDCs to have an internal business development contact, who understands both the scientific and business development aspects in order to facilitate such alliances.

Therapeutic Areas of Focus

To attract interest from biopharma partners, academics must understand which therapeutic areas are currently of interest to biopharma (highlighted in **Figure 7**[33]). These interests are driven by market demands, and thus are continually evolving. While all top 10 biopharmas by global revenue expressed interest in academic partnerships in oncology, cardiovascular, and metabolism, less than five companies expressed interest in ophthalmology, inflammation, and rare diseases. This illustrates the importance of having a current understanding of the potential partners for one's research.

CONSIDERATIONS

Although each biopharma has a different approach towards academic partnerships, there were three consistent themes that arose in our biopharma interviews.

First, industry-ADDC partnerships rely heavily on personal relationships and networks (see **Appendix G** for industry-ADDC network map). Therefore, a business development manager is critical to developing strong relationships with biopharma, and soliciting ideas and feedback on projects in their academic pipeline.

Second, industry does not seek to leverage academic capabilities that they do well internally (i.e., Medicinal Chemistry), and academia should focus on identifying its unique strengths that provide them a competitive advantage. For example, Biogen mentioned their interests lie in finding new targets, novel biology, and drugs for the so-called "undruggables." Pfizer, on the other hand, looks for novel science where most have given up, or a solution seems intractable. J&J suggested that screening higher risk targets could be attractive to industry. As alluded to above, biopharma believe they have a significant advantage in chemistry, and therefore, most academia developed chemistry data is not perceived to have high value by industry.

Finally, industry-academic partnerships are contingent on reproducibility. Without reliable, accurate data, industry is unwilling to engage with academia. In 2011, Bayer scientists issued a report indicating that 67% of published data brought in house could not be reproduced,[34] an issue consistently reiterated during the team's interviews with biopharma representatives Therefore, academic researchers must strive towards generating industry quality data in order to foster industry partnerships.

BIOPHARMA VENTURE CAPITAL

TRENDS

2014 was a banner year for biopharma venture capitalists (VCs) with significant growth in fundraising, mergers & acquisitions (M&A), and initial public offerings (IPOs). Biopharma VCs invested $6.0 billion in US biopharma companies, a 32% increase from 2013.[35] Biopharma VC investments are driven by:

- capital availability in the fund
- perception of unmet medical need
- exit opportunities via acquisition
- exit opportunities via public markets
- the overall regulatory and reimbursement environment[36]

VCs have been actively raising capital for new funds for the first time since the financial crisis in 2008. Collectively, top biopharma VCs have raised $4.2B in 2013 and 2014.[37] Moreover, private funding for biopharma increased 50% in 2014 – an inflow of $9 billion.[38] With this increased liquidity, VCs are willing and able to make new investments in promising startups.

VCs have found increased success by investing in compounds that address unmet medical needs. Specifically, compounds for orphan designations are more likely to gain approval if successful, and thus command a high valuation. Of 98 biopharma M&A deals from 2008 –

2012,[39] 40% included a compound for an orphan designation.[40] Because of the high need for orphan therapeutics, VCs will continue to see high promise in these investment opportunities.

Acquisition activity by biopharma companies has been increasing since the financial crisis. Announced biopharma M&A deals increased 10% from 2013 to 2014, totaling $40.7B. Moreover, there were 377 announced transactions, 37 more than the previous record in 2006.[41] Seeing the possibility of an exit to pharma companies, again, increases VCs' willingness to invest.

2014 also marked an unprecedented increase in exits through IPOs. In 2014, there were 62 biopharma IPOs, double that of 2013, and 6X-12X the past 10 years.[42] These deals transacted for nearly $4.5 billion dollars.[43] Moreover, IPOs are shifting earlier in the drug discovery process. From 2008 – 2011, there were no Preclinical or Phase I biopharma IPO exits. In comparison, nearly 30 Preclinical or Phase I biopharma companies exited through IPO in 2012 – 2014.[44] VCs see IPOs as a positive alternative to an exit via acquisition.

As with the large biopharma companies, the regulatory and reimbursement landscape remains challenging, and ever evolving. Nonetheless, biopharma VCs have navigated around these hurdles by pursing orphan indications, where there is more regulatory and reimbursement lenience.

In sum, biopharma VCs significantly benefitted from macroeconomic factors, which have generated new capital for VCs, as well as increased exit opportunities from both M&A deals and IPOs. As a result, many early stage VCs are bullish about engaging with academic projects to take advantage for the renewed capital liquidity.

APPROACHES

Biopharma VCs engage with projects across the drug discovery and development timeline. Over the past 10 years, 30% of VC investment has gone into projects in the preclinical phase, 20% has gone into projects in Phase I, another 30% has gone into projects in Phase II, and the remainder has gone into Phase III and beyond.[45] The team primarily interviewed VCs who invest in preclinical drug discovery, though even in this realm, we found a range of investment strategies, where some engaged with a project once a hit had been identified, while others did not engage until the candidate selection stage.

With regard to therapeutic area and approach, VCs exercise a range of strategies. From 2004 – 2013, metabolic, ophthalmology and platform therapeutic areas have gained increased VC funding, while other therapeutic areas have remained stable or declined in funding.[46] Given the 32% increase in VC funding from 2013 to 2014, it is likely that all therapeutic areas have benefitted from the uptick in capital.

Consistently, 78% of VC funding has been in novel targets (i.e., NME with no prior regulatory approval).[47] Through interviews, the team discovered that some VCs exclusively

invest in novel targets, whereas others invest in repurposed molecules. Similar to biopharmas, VCs rely primarily on publications and personal relationships to identify deals.

Early Discovery VCs – Engaging Pre-Lead

VCs that invest in early stage drug discovery projects are primarily interested in the novelty of the pathway, druggability of the target, and early efficacy expectation. These VCs will typically engage once promising hits have been identified.

While novelty can be a subjective concept, VCs consistently expressed that a novel target should be bold and surprising, rather than obvious. Moreover, there should be a clear mechanistic rationale for the target. VCs have found that having a strong story for how the target impacts the disease pathway helps attract resources (such as talent and funding) to the project. To validate the novelty, the data package should include robust in vitro and early in vivo data demonstrating the mechanistic rationale.

VCs prefer easily druggable targets because of the high risk involved with the early discovery phases. As such, the data package should identify a decent molecule or family of molecules that could be pursued. Importantly, these molecules should offer high specificity, as this is an early hurdle compounds must surpass. To demonstrate the druggability, VCs want to see sufficient structure-activity relationship (SAR) data to have enough "shots on goal." The data package should demonstrate the compound binding to the crystal structure.

Lastly, early discovery VCs want to understand how the project will demonstrate efficacy in later stages of the project. As such, the project should have a well-validated target product profile specifying how the team will evaluate biological efficacy and specificity. In particular, there should be a reliable biomarker that can be tested to determine the efficacy and specificity in later stages. Aside from these characteristics, early discovery VCs have little interest in additional data. For example, they do not perceive lead optimization as a "value creation" phase of the project, and feel lead optimization should be performed outside of academia in order to maximize resources for the process, thereby expediting the turnaround time on the project.

Late Discovery VCs – Engaging Post-Lead

VCs that invest in late stage drug discovery projects are interested in similar themes as the early discovery VCs, in that novelty, druggability, and efficacy are critical. However, these VCs look to engage with a project once a "lead-like" compound has been identified. These VCs expect robust lead optimization to have happened and a promising candidate has been selected. Late discovery VCs want to avoid spending money on lead optimization, given the high burn rate during this process.

Biopharma Accelerators

Biopharma accelerators support biotechs by providing capital and resources to quickly de-risk the project and progress into clinical trials. Biopharma accelerators take many forms. Some are stand-alone entities that have received VC funding to accelerate projects (i.e., Cydan, Accele Biopharma, and Accelerator). Others are funded through disease-specific

accelerators, such as Leukemia and Lymphoma Society Therapy Acceleration Program (TAP) or the Neurofibromatosis Therapeutic Acceleration Program (NTAP).

In both models, the accelerator has collected a group of experts and resources to quickly identify necessary experiments to reach a "go/no-go" decision in the project. Projects are typically selected when they are 12-18 months from entering clinical trials. During this time period, the accelerator may leverage CROs to perform critical preclinical development in Pharmacology, Chemistry, Manufacturing and Control (CMC), and Toxicology. Through these projects, the accelerator will prepare the project to spinoff into its own start-up or license into a biopharma company.[48]

For academic projects, accelerators can be important partners to bridge the gap between preclinical developments to clinical trials. Academic drug discovery projects often face hurdles in this phase, given the limited funding options, and many of the CMC studies cannot be performed within an academic institution.

Learning to Innovate from Biopharma Venture Builders

Third Rock Ventures and Flagship Ventures are known to be exceptional biopharma VCs with significant innovation capacity. In addition to acting as a traditional biopharma VC, Third Rock and Flagship have a venture builder arm, where they create their own startups by rigorously exploring whitespace opportunities and vetting these ideas with industry experts. Since 2004, Flagship Ventures has launched eight companies through this model, one of which has exited via an IPO.[49]

In these venture builder models, the company will define a whitespace for which they plan to innovate a solution. They will assemble an interdisciplinary team of internal and external experts, such as scientists, IP lawyers, biopharma business professionals, etc., and work to develop ideas that address the defined whitespace challenge. During this phase, the team will begin broadly, before narrowing down to 5-6 viable ideas. As these ideas begin to coalesce, the team will seek out advice from a broader group of experts to provide feedback on these ideas. During this process, Third Rock will assign 1-2 FTEs alongside a handful of advisors and consultants to move the project forward. Through the feedback process, the team will iteratively adjust the idea and narrow down to 2-4 concepts.

To further vet these concepts, the team will identify 1-2 key experiments to validate the concepts. At this stage, there are 5-10 FTEs assigned to the project, as well as consultants and entrepreneurs-in-residence. Based on the outcomes of these experiments, the team will narrow down to 1-2 ideas, which will then get funded through a Series-A investment.

Overall, this process will take 2-4 years. Venture building hinges on iterative interdisciplinary conversation and exploration to continually test the viability of a biopharma innovation. Venture building is beneficial because the project's participants are not enamored with any one idea, but rather eager to uncover the truth behind the whitespace area as a whole. Moreover, venture building is a cost effective innovation process, as the team aims to understand the details of the project before heavily investing.

CONSIDERATIONS

Similar to biopharmas, academics should prioritize relationship building with VCs as a means to gain feedback on projects, as well as open the door to deals. In particular, VCs are well networked in the biopharma community, as they interface with innovators, both in and outside of academia, as well as with biopharmas through the M&A process. As such, relationships with VCs can yield positive network effects to an entire organization.

Similarly, academics should be aware of the perceived value add phases within a drug discovery project. Before significantly investing in a research project, academics should validate that the data will uncover an important aspect of the target or compound. Additionally, data reproducibility is of pinnacle importance, as irreproducible data quickly diminishes trust with the biopharma VC community.

As a separate area of consideration, ADDCs should take note of the Third Rock and Flagship venture building strategy. While academia may lack deep coffers for funding, it is abundant in thoughtful and intelligent experts across disciplines, resources and knowledge that could be leveraged as a method to iterate on and refine a project, rather than taking the brute force approach of testing everything in a lab. In fact, the team learned from Stanford Spark about how they were able to reach a lead candidate by generating roughly 100 compounds, rather than the thousands typically created in industry. Skeptical about the process, an industry scientist could not find any flaws in the candidate when reviewing the candidate. Similarly, ADDCs should consider thorough interdisciplinary vetting of the project in order to optimize the path forward.

ACADEMIC DRUG DISCOVERY CENTERS - BENCHMARKING

TRENDS

Over the past five years, the number of ADDCs has grown from 78 in 2011[50] to 101 as of 2015[51], representing a 29% increase over the past 5 years. Despite the proliferation of these centers, primary research has shown that no single ADDC has hit upon the right model for sustainable success (if measured by number of licensed and/or FDA-approved compounds). This is partly due to difficulty in measuring impact of policy or programs in an industry where the path to FDA approval can take over a decade. In addition, factors such as the high failure rate inherent in the process and lack of funding, make gathering best practices to be a difficult isolate.

In addition to the rising number of ADDCs, there is also variation in structure and services. The four main models of academic drug discovery centers are accelerators, core services facilities, collaborations, and hybrids. Accelerators function primarily as a funding mechanism for proposals and generally do not provide core services, education, or other administrative support. Core services facilities function as a source for PIs to receive high-throughput screening (HTS), pharmacokinetics (PK), medicinal chemistry, and/or structure based drug design services, but generally not funding or guidance. Collaborations are ADDCs spanning multiple academic institutions who share resources and engage in

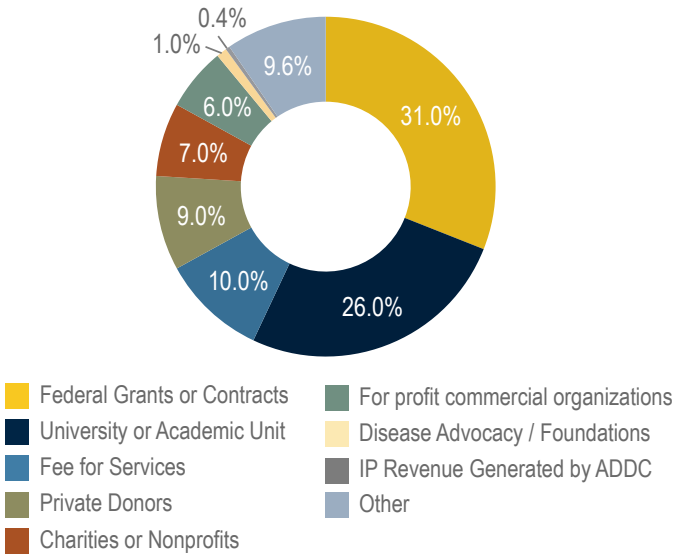
collaborative projects, and are often based on geographic proximity. Lastly, the hybrid ADDC model includes components of core access, funding, education, and guidance.

ADDC SURVEY RESULTS AND TAKEAWAYS

A survey, based on the one detailed in "US Academic Drug Discovery"[52], was created to gauge sources of financial support, services offered by the center, therapeutic areas and approaches of focus, and the components that drive the ADDC's mission. Of the 102 ADDCs it was sent to, 48 responded. The key finds are shown below:

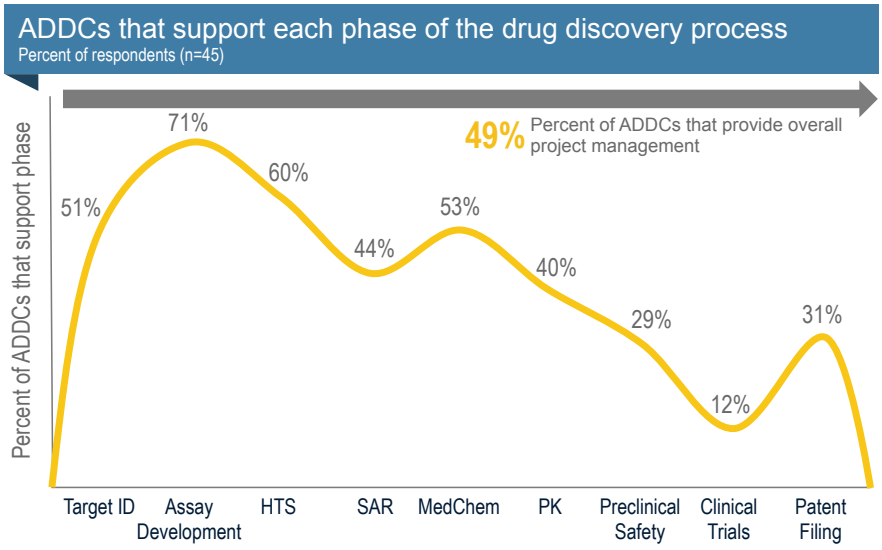
Median Number of Tenured Faculty Receiving Support: 23
Median Annual Operating Expense: $650,000
Median Annual Budget: $850,000

Figure 9: Breakdown of ADDC funding sources)



The two main financial support sources for ADDCs are federal grants and university funding, while IP revenue and disease advocacy groups were the smallest sources (see **Figure 9**)

Figure 10: Areas of the drug discovery process supported by ADDCs (n=45)

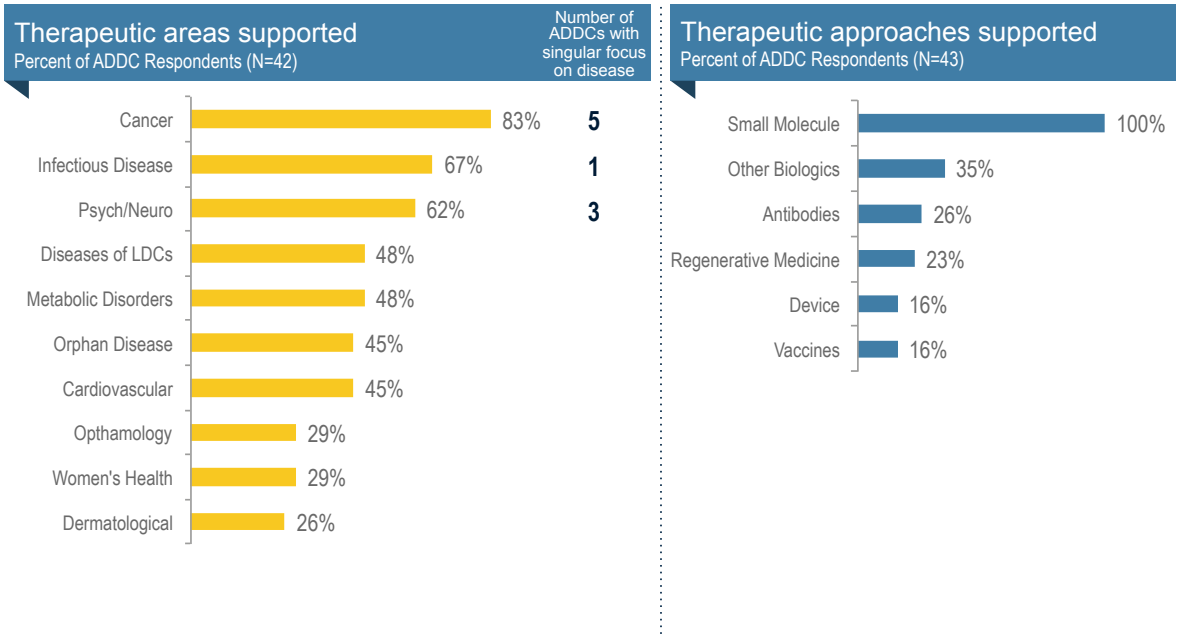


When it comes to the drug discovery process, the stage that is most supported by ADDCs is primary assay development, while over 50% of ADDCs support target identification, high throughput screening, and medicinal chemistry (see **Figure 10**).

Cancer is the most widely supported therapeutic area by ADDCs, followed by infectious disease and psychiatric/neurologic

disorders. Cancer was the sole therapeutic focus for 5 ADDCs, while 4 focused solely on neurologic disorders (see **Figure 11**).

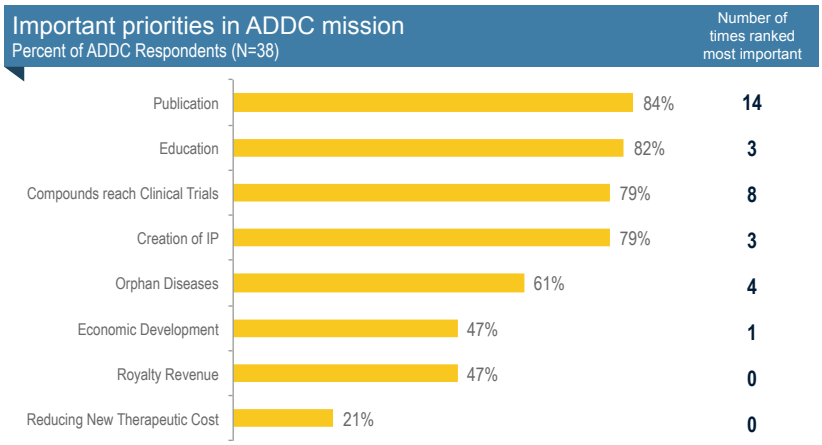
Figure 11: Therapeutic areas (n=42) and approaches (n=43) supported by ADDCs



All of the ADDCs supported small molecule discovery, while 61% of ADDCs supported biologics (combining antibodies with nucleic acids, peptides, etc.) (see **Figure 11**).

The most frequently cited component of ADDC missions was "advancement of science through publication", followed by "training of graduate and/or postdoctoral students." The respondents also ranked these mission aspects based on importance, and the component ranked first most often was the "advancement of science through publication", followed by the "progression of agents to clinical testing." (see **Figure 12**)

Figure 12: Priorities in ADDC mission (n=38)



In terms of obstacles, 97% of respondents cited lack of funding/sustainability. Two additional obstacles cited by multiple respondents were the need for more PI education on the drug discovery process and a greater need for university support.

ADDC CASE STUDIES

Through our primary and secondary research, we came across ADDCs with differing structures, goals, focus, and missions. Below are some examples that showcase the various ADDC approaches (additional case studies can be found in Appendix H).

Stanford Spark

Background: Established in 2006 within the Stanford School of Medicine, SPARK is a translational research program with a threefold mission of helping PIs move their discoveries from bench-to-bedside, educating PIs on the translational research process, and developing cost-effective approaches to drug development[53]. Funding for the program mainly comes from a combination of university funds and disease advocacy groups, along with some federal grants. SPARK is an example of a hybrid ADDC model, offering funding, project management, industry advice, and education.

Program Structure: The program kicks off with an annual request for proposals that center around an unmet medical need, involves a novel approach, and has the potential to advance to clinical trials or licensing within 2-3 years of SPARK support.

Projects are picked for funding (up to $50,000/year for 2-3 years) by a selection committee comprised of SPARK management, academics with translational research or industry experience, and people from industry with drug discovery expertise. Once selected, a SPARK project manager is assigned to help the PI's team develop a target product profile, assess project progress and milestones, and troubleshoot roadblocks. SPARK project teams attend education seminars, give quarterly project updates to SPARK management and industry advisors, and receive the yearly funding based on participation in these activities and meeting milestones. The industry advisors (who are all volunteers) provide consultation and feedback to the SPARK teams on project progress and in areas such as the core stages, regulatory environment, clinical trials, and business development. Based on primary research, it is the education, program management, and guidance from advisors that are the most valuable aspects of the SPARK system, rather than the funding.

Educational Component: SPARK has also built in an education requirement for all of its fund recipients. In order to receive funding, PIs are required to attend weekly educational meetings, which begin with teams learning about the drug discovery process and IP, along with creating a target product profile. Weekly sessions alternate between project updates and drug discovery seminars taught by SPARK advisors. The attendees of these meetings are advisors and SPARK project teams. As a result, all teams learn together at the seminars and from each other's drug discovery progress and roadblocks during the project updates.

Key Takeaway: Though lack of funding is a widely cited obstacle by both ADDCs and PIs, it is worthwhile to examine all the facets that fuel project progress. The complexity of the drug discovery process necessitates other areas of support for PIs, such as expert advice, education, and overall project guidance (factors to be considered for an ADDC program).

Harvard Blavatnik Biomedical Accelerator

Background: Established in 2013 after raising $45 million in alumni donations ($35 Million from one donor), the Blavatnik Biomedical Accelerator (HBBA) is part of Harvard's Office of Technology Development. The original HBBA, launched in 2007, was re-established in 2013 after the single donor gift of $35 million. HBBA supports therapeutics, platform technologies, devices, and other biomedical technologies. After reviewing proposals, finalists are awarded either a development grant of $300,000 over a 2-3 year period or a smaller pilot grant over 1-2 years, depending on the development stage of the project.

Funding Experiment: Although 20% of royalty revenues will go back to HBBA (not taken from the inventor's royalty portion), the program is viewed internally as an experiment. The $35 million is allocated over seven years to fund projects, provide project management support for the PIs, and foster alliances with potential industry partners.

Key Takeaway: In the course of primary research, HBBA was one of two ADDCs that seemed to view their operations as an experiment. Recognizing that the drug discovery process involves many moving pieces, HBBA has an external advisory committee comprised of experts from industry and VCs, offering guidance on project progress, and helping identify CRO options for PIs. However, the HBBA leadership also recognizes the high failure rate inherent in the drug discovery process and has set milestones for its own program in order to measure the success of the operations and better utilize the donor gift it has been given.

The Role of CROs in Academic Drug Discovery

Biopharma R&D is increasingly relying on CROs to outsource drug discovery and development in preclinical and clinical stages.[54] However, their role within ADDCs is more complex. Our primary research with ADDCs has yielded mixed reviews on their usage, ranging from none at all to targeted usage, depending on the ADDCs' capabilities. CRO services are mainly utilized for the iterative, operational portions of the drug discovery process, known as the core functions, which are HTS, structural biology, Medicinal Chemistry, and PK. The primary reasons ADDCs utilize CROs is when core capabilities have reached capacity, or if the ADDC lacks such capabilities. However, balancing this usage is the greater expense, compared to in-house services and need for oversight.

PROS VS. CONS OF USING CROS

The pros of engaging with CROs are dependent upon capacity, capability, and collaboration with academic institutions. If there is a bottleneck for project progress within one of the core services, supplementing one's in-house capacity with a CRO to generate data and move forward within the drug discovery process can be useful. Concurrently, if the ADDC does not have the necessary services at all, it also makes sense to outsource those needs to

a CRO fill that capability gap. In addition, if the PI is investigating a therapeutic area in which there aren't in-house experts for advice on types of animal models to use, it would be useful to engage CRO services with expertise in that therapeutic area. A reputable CRO could also be an outside source of data validation, a key step when engaging with possible industry partners or VCs. Finally, there could be scope for collaboration between the smaller in-house core labs and the larger infrastructure of a CRO, especially as a means to further build expertise of academic core labs.

Conversely, the cons of engaging with CROs center on quality, expense, and management for the ADDC. It is crucial to work with a reputable CRO for research practices and data management, for fear that the data generated by the service could be called into question, or data confidentiality could be violated. However, the caliber of the CRO must also be balanced by its cost, and herein lies the biggest roadblock for ADDCs. Early in the drug discovery process, many projects are funded via grants or seed funding, which often cannot cover the cost of the iterations needed to generate data for compounds. In addition, due to its' business model, CROs are motivated by maximizing the number of services they can provide, and as a result, this may not serve the best interests of PIs who are trying to keep costs down.

Applicability to the University of Michigan & CDNM

CDNM is one of the few ADDCs that has in-house core lab resources for its' PIs, led by industry experienced experts. This gives PIs the opportunity to both collaborate and consult with core lab directors, especially since most PIs do not have expertise in all four core resources. However, over the course of primary research at the UM, all four core labs are at or near capacity, with medicinal chemistry as the primary bottleneck for PIs. As a result, there is scope for working with CROs, especially if the core directors offer guidance on the process and output of the CRO services.

CONSIDERATIONS BEFORE ENGAGING WITH CROS

Based on primary research with both ADDCs and industry, we have found that the quality and reputation CROs is of utmost importance, so proactively reaching out to industry or VCs for CRO recommendations would be a useful first step in due diligence. Another crucial factor to a successful CRO engagement is the necessity of a project manager or expert that oversees the relationship with the CRO. Although CROs have expertise in carrying out the individual process of PK or medicinal chemistry, a manager (core lab director or external consultant) with core expertise is necessary to guide the process and manage the CRO relationship. Other considerations that should be taken into account are the location of the company, strengths of the CRO (as opposed to just the breadth of services being offered), and responsiveness of the scientists and management within the CRO to its' customers.

Drug Discovery at University of Michigan

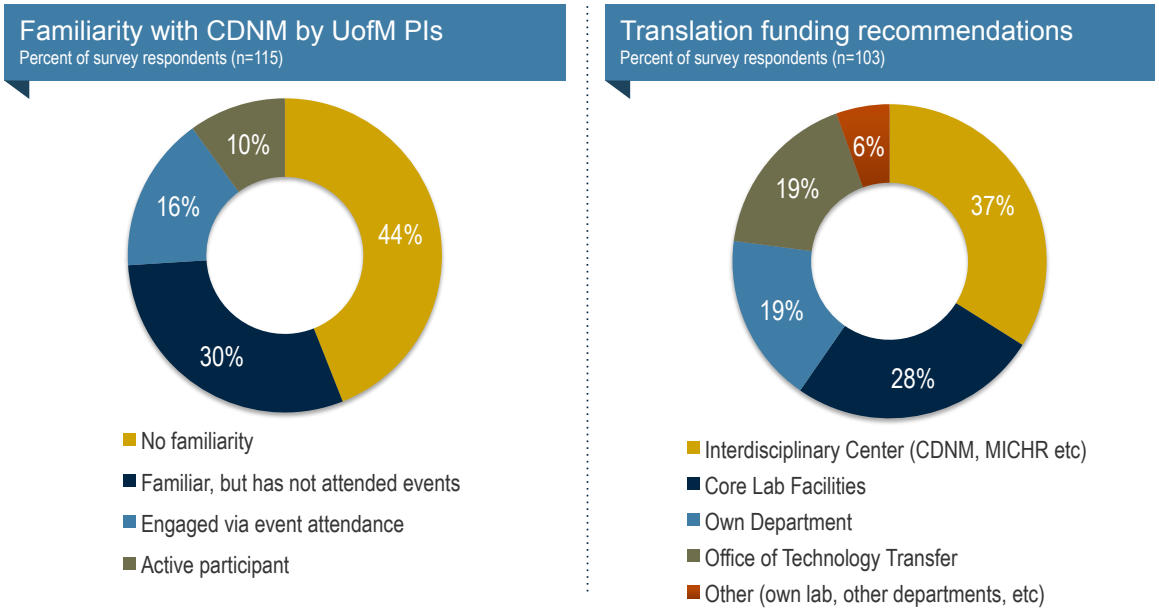
PERSPECTIVES FROM PRICIPAL INVESTIGATORS

We created and distributed a survey to UM faculty in Biological Chemistry, Biomedical Engineering, Cell & Developmental Biology, Human Genetics, Internal Medicine, Microbiology & Immunology, Molecular & Integrative Physiology, Pathology, Pharmacology, and Pharmacy departments. The survey, targeting faculty interested in translational research, was meant to gauge the level of awareness of drug discovery programs, their translational funding approach, and what activities PIs spend their time on in their labs.

PIs interested in translational research are most aware of Michigan Institute of Clinical & Health Research (MICHR) and the Office of Technology Transfer (OTT). 57% of respondents are engaged with or actively participating in MICHR, while 53% of respondents did the same for OTT. In contrast, 77% of respondents either had no familiarity or did not attend events for CDNM.

65% of PIs would allocate additional translational research funding to an interdisciplinary center and core labs, highlighting PIs' interest in internal drug discovery programs, and the value of the core labs' support to PI research (see **Figure 13**).

Figure 13: Awareness of Translational Research Programs at UofM (n=115)



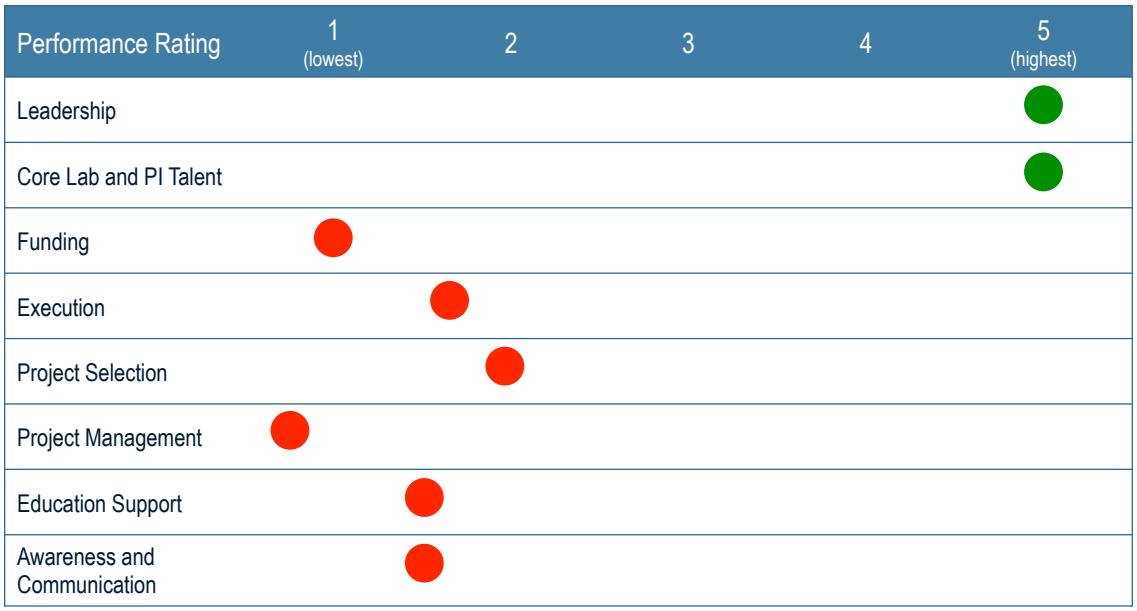
For therapeutic areas, cancer was the disease area with the most focus (31% of PIs), followed by neurologic disorders and cardiovascular disease (20% each). In terms of therapeutic approach, most PIs focused on small molecule (56% of PIs), followed by biologics (both antibodies and peptides, nucleic acids, etc), with 30% of PIs.

PIs ranked services they felt were most important to fostering drug discovery at UM. 62% indicated that opportunities for funding were the most important, while the next most important was advancement of science through publication (7%). Creation of new companies and/or job creation, along with industry connections were least important. Unsurprisingly, 91% of respondents mentioned funding as a major obstacle to drug discovery expansion at UM, although other responses included lack of: collaboration and support for drug discovery, technical resources/expertise, and drug discovery education.

CENTER FOR DISCOVERY OF NEW MEDICINES – CURRENT STATE ASSESSMENT

Before making recommendations for CDNM, the team assessed the current capabilities of CDNM across several areas. The assessments were made on a relative basis, utilizing primary research from interviews with other ADDCs and from the ADDC survey conducted in order to establish reference points within each category. The rankings were discussed and agreed upon with CDNM's Director (seen below in **Figure 14**).

Figure 14: Current state assessment of CDNM capabilities



RECOMMENDATIONS

PROGRAM STRUCTURE

Although there is no surefire way to ensure translational success, certain functionalities within academic drug discovery can be improved to better enable opportunities for collaboration, build momentum for promising projects, and ultimately strengthen bridges between basic and translational research. As a result, based on feedback from industry and VCs regarding their experience with academia, along with best practices from ADDC directors, we are proposing a program structure based on project filtration, progress management, and industry alliances.

Selection

Due to the high failure rate within drug discovery and the limited funding that CDNM is able to provide, vetting projects that receive funding is crucial. Although early stage projects are highly variable in nature, which makes picking "winners" difficult, there should be standards in place to encourage high quality proposals and a diverse review board to verify them. We recommend that a diverse scientific advisory board (SAB), made up of representatives from industry, startups, clinicians, researchers, and intellectual property (IP) experts, be convened to best guide which proposals should be awarded with funding. Having diverse viewpoints on the scientific rigor, industry interest, IP potential, and clinical viability will increase the projects' likelihood of gaining future funds.

Navigation

We recommend appointing research navigators to maintain project momentum, guide PIs, and bridge gaps. These navigators would guide PIs throughout the drug discovery process by identifying and coordinating resources to move projects forward, monitor adherence to the project plan and milestones (or adjust plans as necessary), and smooth collaborations between PIs and core lab directors during the course of a project. The research navigator would act as a representative of the project as a whole, whose responsibilities could also include setting realistic expectations and interfacing with industry or outside partners as needed. As a neutral party in the process, navigators would be well positioned to provide a holistic point of view of project needs, by consulting with therapeutic experts on appropriate animal models, seeking external funding sources, engaging with core lab experts on data, or interfacing with CROs. A possible partner to the navigator would be core lab directors, who would act as consultants in evaluating the efficacy of the core data being generated for the project, and be compensated for their time by CDNM. Based on primary research, we recommend that navigators be able to "speak the language" of both science and industry (though scientific expertise in the therapeutic area of the project is not necessary for effectiveness). The estimated capacity of projects per navigator is three to four, though that number is dependent on project complexity (based on the project management frameworks in place at NINDS, UCSF, SPARK, and the Broad Institute).

Alliances

The third recommendation for CDNM's program structure is dedicating resources to industry alliance management. A consistent theme from our primary research was the critical role that networks and relationships play when it comes to industry alliances. While geography plays a role in such alliances, the takeaway from our research was the importance of industry relationships for academic institutions to gain industry support. Therefore, appointing an industry alliance/business development manager would be crucial for CDNM and the UM drug discovery ecosystem. This manager would play a role in connecting promising projects to private sector partners and increase the center's profile in industry and VC business development circles. An alliance manager would broaden CDNM's network, and act as CDNM's representative at industry and academic conferences.

EDUCATION

Drug discovery requires diverse fields of expertise throughout the process including biologists, chemists, pharmacologists, finance, business development, law, etc. However, basic science researchers rarely work across disciplines, and are traditionally incentivized to achieve individually focused results (such as grants and publications), rather than collaborative and team-oriented work. As a result, basic science researchers require technical education on the drug discovery process, as well as education on servant leadership, collaboration, and managing team dynamics.

Strong educational programming will pay dividends to CDNM over time by facilitating community building around translational research, and thereby engender bottoms-up support for CDNM. In interviews with other ADDCs, the team learned that interdisciplinary translation programs, such as CDNM, require both top-down support from administration, as well as bottoms-up support from faculty, postdocs, PhD students and staff. Because university administrators are often influenced by the campus opinions, strong support for CDNM from the UM life sciences community should lead to ongoing funding and support from the administration. Many other ADDCs have garnered funding and support from top administration, as the ADDCs had received strong bottoms-up support as well.

Curriculum Development

CDNM should develop its curriculum through a participatory approach that considers the interests and priorities of the faculty, postdocs, PhD students and staff at UM. By including the voice of the life science community, CDNM will have a higher chance for developing programming that will garner campus support.

In practice, CDNM should interview faculty, postdocs, PhD students and staff to understand their interest and priorities for learning opportunities related to team science and drug discovery. Moreover, CDNM should seek to co-develop educational programming with other life sciences departments. By collaborating with other departments, CDNM will demonstrate its eagerness to create a collaborative translational research community.

Along these lines, CDNM should strive to create interactive educational opportunities, such as simulations and case-based experiences, rather than didactic lecture formats. Research has shown that medical professionals retain information learned through case-based experiences better than didactic lectures, and are more engaged through interactive, rather than passive learning opportunities.[55]

CDNM Grantees

CDNM should establish a required, bi-weekly education curriculum for project team members who receive CDNM grants. In these sessions, CDNM would offer technical guidance for each stage of the project, as well as a variety of co-learning opportunities, where teams would update one another on their latest project status. During the technical sessions, CDNM would guide the cohort through the next phases of their respective projects. Additionally, some sessions could focus on the business and legal sides of the

development process. Educators for these sessions could be a combination of the CDNM Director, core leaders, experienced translational researchers at UM and external experts.

At least one project team member would be required to attend the event, and CDNM funding should be contingent on participating in the educational programming. The events would be open to the public (although required to sign a confidentiality agreement), so that other interested parties could learn from the sessions.

Through interviews, the team learned that faculty are stretched for time and may not be willing to allocate time to these learning sessions. However, the team reconciled that in order to move projects forward, the PI must be committed to the project's success, including educational programming. In fact, some interviewees at UM confirmed that when PIs are committed to a project, they will go above and beyond to see the project through. The team considers these anecdotes as a testament to the fact that academia require a supportive community for translational researchers.

Post-Docs and PhDs

Through interviews, a recurring theme was that postdocs and PhDs are often more enthusiastic about translational research than tenured faculty. Even when a PI is engaged with translational research, the project work is typically done by postdocs and/or PhDs. Students are an important group in the translational research community. CDNM leadership should solicit programming ideas (e.g., mentoring opportunities, networking events with industry, and professional development retreats/dinners) from postdocs and PhDs to help them gain a sense of community.

CDNM should also explore internship and/or rotational opportunities in industry for post-docs/PhDs as a way to gain the industry perspective on drug development (similar to Stanford's ChEM-H/Novartis pilot). After the 2014 pilot, Novartis chose to double the number of 2015 internships, something Stanford benefits from by improving PhD acceptance rates and increasing drug discovery fluency on campus.

OPERATIONAL STRUCTURE

Currently, CDNM lacks coordinated execution of its vision. While the core lab leaders are involved with supporting CDNM projects, in earlier CDNM funding rounds, they were not part of the selection process, resulting in selections of poor quality projects that were not well prepared to be taken on by the core lab. Additionally, many projects were stalled because some of the discovery work needed to be completed by the PI lab. However, since CDNM funds are directed solely towards core lab use, the PI's lab did not have funding to bridge that gap between the work in the lab and the core lab.

All in all, the current operational structure led to poor project selection and fractured execution. CDNM should address both of these issues in order to improve the drug discovery process at University of Michigan.

Support Core Consultations

CDNM benefits from having a strong leadership team in its core labs, a component validated by several interviews as critical to the success of ADDC projects. However, today, the core lab leaders spend a lot of time consulting and advising on projects without compensation, resulting in the core leaders being stretched thin in their efforts, thus slowing down the projects' progress. Some core labs have started to charge clients on project design consultation, potentially disincentivizing PIs from consulting with the core labs on projects. Therefore, CDNM should support 10-20% of the core labs' costs to cover consultations on drug discovery projects.

Motivate PI Participation

CDNM should shift how it disburses funding to grantees. Rather than funding through recharge, CDNM should dole funding to PIs through reimbursement. That is, when PIs use certain materials and supplies for research on a project, the lab can then request reimbursement from CDNM for those items, potentially avoiding project funding gaps.

FUNDING

It should come as no surprise that funding mechanisms/opportunities were consistently mentioned as the biggest hurdle for continuing drug discovery research by all stakeholders interviewed, but especially from academic institutions. In order for an academic institution to be successful in drug discovery and to truly be viewed as a leader in that field, buy-in from both the top-down, as well as the bottom-up, is critical. As Stanford's ChEM-H program put it, "with support from one side, the program can stay afloat, but support from both ends is what's necessary for it to excel and be successful." This support also must be continuous, beginning with financial assistance, but sustaining the growth and success of the program relies on the leaders of the institution substantiating their support by advocating for the program. This type of holistic support system separated the programs that seemed to do just enough to get by from those that were excelling as an ADDC.

While some programs were excelling from the holistic support system described above, there were others that were initially launched from large donor funding, and have implemented a policy that could distribute royalties to their center in 5-10 years. Those that operate in this fashion (i.e. Harvard Blavatnik Center, receiving 20% of the royalty revenue allocated to the university's general fund) fully acknowledge that their center is not sustainable today, and view their center as experimental, hoping their endeavors pay off before their donor funding runs out. While the team does not advise taking this approach for CDNM, there were several pros and cons that were considered:

Table 1. Pros and Cons Considered for Royalty Policy Change

PROS	CONS
• Creates potential for financial return • Does not take share from PI's potential return • Illustrates support from leaders of university	• Alienates CDNM, viewed as monetizing PI's research, and taints CDNM mission of advancing science • Difficult to implement policy change of that impact • Potential to spark rivalry within academic institution

- Current departmental financial support could be cut

To enable CDNM to be successful early and supplement the holistic funding support (within UM), securing initial donor funds has proved to be extremely valuable in the early stages of an ADDC program. In addition to two programs from our interviews (Harvard and the Broad Institute), 15 of the surveyed ADDCs are supported by donor funding.

Other alternatives for funding mechanisms that were less thematic, but are certainly viable alternatives, and currently support several drug discovery programs:

- State funding (i.e. University of Minnesota, University of North Carolina) allocated to support translational research at Michigan universities
- Patient advocacy groups (5 surveyed programs are supported by patient advocacy groups for their programs funding)
- Leverage funding from consortium-type collaborations with MI/Midwest ADDCs
- Sponsored research and industry-academic alliances

SUCCESS METRICS

The success and impact of an ADDC can be difficult to measure, given the amount of time required before one can (hypothetically) assert one's translational research project yielded a new drug compound. Therefore, through interviews with the various stakeholders involved in academic drug discovery, the team has identified several leading metrics of success that align the goals of academia and potential partners/investors, as well as some of the metrics utilized by biopharma and VCs.

Shared Metrics (CDNM, Industry, VCs) Leveraged by all Stakeholders

Number of Publications Generated from CDNM Supported Projects

While publications may not provide any monetary value for industry and VC partners, that was the leading methodology for identifying partnership, licensing, and investment opportunities within academia (7 of 12 biopharma and 4 of 7 VC interviewees mentioned as the leading source for discovering academic opportunities). Some industry partners mentioned that they utilize this as an initial filter to target academic collaborations. This metric also aligns with tenure-tracked professors and researchers, as they are benchmarked against this metric.

IP (Patent) Licenses

Generating quality IP can be extremely valuable for ADDCs, especially when a project has moved further along the drug discovery process and has garnered interest from VCs and industry partners. From the team's primary research analysis, 79% of ADDCs surveyed (n=38) mentioned that IP generation was an important part of their mission, while 3 of 12 biopharma and 3 of 7 VC interviewees mentioned they utilize patent filings to target investment and collaboration opportunities.

Internal (CDNM) Metrics

Number and Amount ($) of Follow-On Grants Generated

Given the capital-intensive nature of drug discovery, every institution interviewed and surveyed acknowledged that their program's seed funding was not intended to be the sole source of funding for the PI's project. However, if the program's support and/or funding enables the PI to be awarded a follow-on NIH grant to advance the project even further (having a multiplier effect), the center should recognize that as a success. Of the 7 ADDCs interviewed, 4 mentioned this as a success metric.

Follow-on funding should be reported as a multiplier effect of CDNM funding. For example, Stanford Spark reported that each dollar of seed funding provided by Spark yielded $5 of follow-on funding – thus demonstrating that the program generated a 5X multiplier.

Other Internal CDNM Metrics of Success to Consider – Number of:

- PIs in drug discovery certificate program (metric for 2 of 7 ADDCs interviewed)
- Different departments engaged with CDNM (metric for 3 of 7 ADDCs interviewed)
- Departments attending CDNM education events (metric for 3 of 7 ADDCs interviewed)
- Projects supported by CDNM (metric for 5 of 7 ADDCs interviewed)
- Collaborations generated from CDNM support (metric for 4 of 7 ADDCs interviewed)

External (Biopharma and VC) Metrics

ADDC Part of Academic Consortium

Not all universities/ADDCs (as individual entities) have the knowledge/expertise, experience, or capabilities to facilitate a drug discovery effort. Biopharma partners and VCs recognize that fact, and therefore, target these established consortium-type alliances (similar to that of QB3 and the Broad Institute) between ADDCs to leverage the power of a broadened collaboration of scientific resources and capabilities (3 of 12 biopharma and 1 of 7 VCs interviewees mentioned this as a metric for targeting academic opportunities).

BRANDING

During the interviews with various UM affiliates (i.e. FFMI, OTT, MICHR, and various PIs), there were several themes that continued to present themselves:

- There is significant confusion on what CDNM does/what it can provide PIs
- It is currently viewed as or part of LSI (exemplified by its website URL - cdnm.lsi.umich.edu), contributing to the lack of understanding of CDNM
- The "Center for Discovery of New Medicines" is difficult to remember, and the acronym, "CDNM", is even difficult to say
- CDNM can be confused with CCG

While some of these items will be addressed over time, there are a few quick recommendations that the team feels would reinvent CDNM as an internal brand, and enable it to establish its own identity:

1. Rebrand CDNM as "University of Michigan Drug Discovery" (UMD^2)

2. Create a clear distinction between UMD^2 and LSI, starting with its URL

Doing so will enable the center to signal a fresh start for drug discovery at UM, and University of Michigan Drug Discovery (UMD^2) provides several auxiliary benefits, while resolving several of the current branding issues previously mentioned:

- "University of Michigan Drug Discovery" clearly depicts the strategy of the center, and articulates the value that the center can provide
- UMD^2 resolves the colloquial clunkiness that hampers the CDNM acronym
- UMD^2 links drug discovery to "MD" (doctors), as well as Ann Arbor (A^2)

RISKS & MITIGATION

Implementation

CDNM should gradually implement this plan (or aspects of it) over the next 1-2 years, so as to not push too many new things at once (both from a center identity concern, as well as budget considerations). Establishing a program structure and internal identity should take priority, with services expansion following as suitable.

Obtaining Sustainable and Diversified Funding

Implementation of our recommendations requires CDNM to increase its budget, and extensively expand its services, with hiring research navigators and alliance manager. To ensure that CDNM's funding does not deplete rapidly, they should work to create multiple sources of funding. In addition to reducing funding risk exposure, gaining financial support internally (from other UM schools, as well as university funds) illustrates the holistic top-down and bottom-up support for CDNM at UM.

Utilizing CROs

While CROs have been successfully utilized at other ADDCs, they must be utilized strategically. They may not work for all PIs or projects, because of costs or a culture perspective. Once PIs begin to understand the benefit of CROs and how to effectively collaborate with them, they can be gradually scaled up throughout the program.

Rebranding of CDNM

As described previously, CDNM currently faces difficulty with its internal identity, underscoring the importance of future branding tactics. However, without a clearly articulated mission and value proposition, CDNM might face similar issues. To avoid such issues, CDNM should clearly and strategically communicate its mission to other UM support programs, academic leaders, faculty, postdocs/PhDs, and PIs at UM.

IMPLEMENTATION PLAN

While the team's recommendation requires CDNM to expand its operations extensively over time, to be successful in the short term, we've made recommendations for next steps to take place over the next two years.

Next 6-12 Months

As first steps to bolster its position as the core drug discovery entity at UM, CDNM needs to establish its mission and increase its brand equity within the university. This can be obtained by broadening its education offerings, as well as continuing to strengthen its network with other UM programs. By doing so, PIs and other academic units within UM will become aware of CDNM, and look to it for not just financial support, but education and mentorship for their drug discovery projects.

Year 1 – Year 2

Once CDNM has positioned itself within the university and has support from the bottom-up, its next focus should be on expanding its services, and recruiting a research navigator to support drug discovery projects. As the university recognizes that CDNM is serious about facilitating drug discovery at UM, this could provide an opportunity to seek funding support from the university leaders, enabling CDNM to gain support from both bottom-up and top-down.

CONCLUSION

Over the course of our seven-week journey, primary research, surveys, and extensive secondary research have given us a greater understanding of the complexity, time, and resources involved in the drug discovery process. Although there currently is no "right" model for sustained success in academic drug discovery, through our primary research with ADDCs, industry, and venture capital, we have been able to isolate key components that will allow CDNM to expand its' capabilities for PI needs and private sector connections.

Ultimately, our recommendations will aid CDNM in becoming a more effective conduit for the talented PIs at the University of Michigan to translate basic research into therapeutics that will improve quality of human life. The proposed strategic plan for CDNM is informed by the current drug discovery landscape and the appetite and resources available for drug discovery at UM. Using this foundation, CDNM can use this optimal program strategy and structure to ensure the center evolves into an effective and efficient ADDC. Moreover, through these recommendations, CDNM can better educate and engage the UM life sciences community in drug discovery, and suggestions for a funding strategy will enable CDNM to sustainably fulfill its mission. By measuring success with the recommended metrics, CDNM will be able to track its progress in drug discovery, ensuring sustainable impact.

APPENDICIES

APPENDIX A – Introduction to Ross MAP Team

Patrick Camalo

- BSE in Industrial and Operations Engineering, University of Michigan
- Quality Management at Owens-Illinois
- Operations and Reliability Engineer at Genentech

Has broken 22 bones

Neha Koul

- BA in Biology, University of Southern California
- Market Planning and Research Analyst at Walgreens

Likes reading presidential biographies

Marianna Kerppola

- BA in Economic and International Studies, University of Chicago
- Corporate Finance at Nationwide Insurance
- Sales and Marketing at Google

Uncanny ability to find four-leaf clovers

Ichiro Hashimoto

- Masters in Mathematics, University of Tokyo
- Government Officer at Ministry of Science and Technology, Japan

Father of 3 year old daughter

APPENDIX B – Project Scope and Timeline

Project Scope
To develop a strategic plan that will position CDNM as a leader in academic drug discovery, we will:

- Explore the current drug discovery landscape by benchmarking CDNM against other academic drug discovery centers (ADDCs) and identifying opportunities for industry partnership
- Evaluate the current financial and operational structure for CDNM and provide recommendations for reaching financial and operational sustainability
- Evaluate the perception of drug discovery at University of Michigan among Principal Investigators (PIs) and assess the brand equity of CDNM
- Provide an educational strategy to incite behavior change and interest towards drug discovery among PIs at University of Michigan

Approach and Timing
Our time and effort will be structured as follows:

Phase 1: Engagement Definition and Preliminary Research (March 9-20)

- Define engagement scope, information needs, timing, resource requirements and constraints
- Perform secondary research to understand the current drug discovery landscape
- Identify key contacts for interviews both at University of Michigan and externally
- Create interview questions guides for target respondent groups

Phase 2: Data Collection at University of Michigan (March 23 – April 2)

- Interview Office of Tech Transfer (OTT), Fast Forward Medical Innovation (FFMI), and Michigan Institute for Clinical and Health Research (MICHR) to understand their roles and responsibilities throughout the drug discovery process
- Interview Heads of each Core Lab (HTS, SAR, MedChem, and PK) to understand project flow, operations and cost structure in their labs
- Interview PIs at UM who have discovered drugs to understand their process and experience
- Develop survey to disseminate to PIs at University of Michigan to understand their perception of drug discovery

Phase 3: External Data Collection (April 6 - 17)

- Interview and survey other ADDCs to benchmark their funding, marketing, operations and performance metrics
- Interview pharma executives in licensing/business development to understand how they form partnerships with academia and what metrics and milestones they look for in licensing or acquisition opportunities

- Interview life sciences VCs to understand what metrics and milestones they look for in therapeutic drug discovery
- Synthesize results from interviews and surveys
- Conduct mid-point review to present findings and preliminary recommendations
- Create outline/drafts of final deliverables

Phase 4: Project Wrap Up (April 20 – 29)

- Finalize research results and recommendations
- Prepare written report and oral presentation
- Present findings to CDNM leadership

APPENDIX C – Interview Guide/Examples

Questions for UM supporters (general/admin, and PIs)

- How do you see the current performance of UM with drug discovery process? What's working and what's not?
- What do you think are necessary to improve UM drug discovery process?
- What UM resources did/do you utilize in the course of your translational research process?
- What type of guidance did you wish you had to make the process easier/smoother/faster?
- Did you engage with FastForward, OTT? When? What areas of support did you gain from either of those support systems? Was there something missing that you feel CDNM would be able to provide?
- What do you know about CDNM? What is your impression?
- What do you think of CDNM's plan to further develop its pilot grant as virtual lab?
- What do you expect for CDNM to foster drug discovery in UM?
- How can UM do better with internal collaboration, education, and industry partnership?

Questions for UM supporters (case studies)

- What were the major obstacles you faced with your translational research? How did you overcome them?
- What UM resources did you utilize in the course of your translational research?
- What type of guidance did you wish you had to make the process easier/smoother?
- Did you engage with FastForward, OTT? When? What areas of support did you gain from either of those support systems? Was there something missing that you feel CDNM would be able to provide?
- What external resources did you utilize in the course of your translational research process?
- When did you start to utilize UM and external resources in the course of your translational research process?
- Do you know about CDNM and if so, what is your impression?
- What do you expect for CDNM to foster drug discovery in UM?
- What do you think of CDNM's plan to further develop its pilot grant as virtual lab?
- How can UM do better with internal collaboration, education, and industry partnership?

Questions for UM Office of Technology Transfer

- What is the typical workflow of OTT with drug discovery process? What's working and what's not?
- How do you see the current performance of UM with drug discovery process? What's working and what's not?
- When is the best timing to start working with OTT?
- Who within UM's drug discovery community do you work with in the course of your evaluation?

- How many proposals do you typically see in this area? What has trend been on that number, if any?
- What proportion of total evaluations are about drug discovery?
- What resources or information would better help you during the evaluation?
- Could you describe details of royalty distribution policy? How is it determined?
- Do you know about CDNM and if so, what is your impression?
- What do you expect for CDNM to foster drug discovery in UM?

Questions for Fast Forward/MICHR

- MICHR: Does your group support the drug discovery process at UM?
- Where do you get funds and how do you allocate them?
- What type of resources do you provide to researchers?
- How many proposals do you receive and how many are granted?
- What kind of educational program do you provide? Who are the target?
- What are working well and what are not with your program?
- Who within UM's drug discovery community do you work with?
- How do you see the current performance of UM with drug discovery process? What's working and what's not?
- Do you know about CDNM and if so, what is your impression?
- What do you expect for CDNM to foster drug discovery in UM?

Questions for CDNM Core directors

- What is the amount of time you dedicate for CDNM projects? Do you work with other groups too?
- What is your opinion on how drug discovery is handled at UM? How could things be improved/what are the biggest hurdles?
- What is the cost structure for each CDNM project and/or drug discovery?
- What is the typical workflow? How do you work with PIs of CDNM projects?
- How do you think CDNM project workflows can be improved?
- What do you think of the CDNM's plan to be a coordinator of PI partnerships to core team capabilities?
- Do you think there is scope and/or time for labs to assist PIs with drug discovery?

Questions for ADDCs

- What is expected of Executive Board and/or Scientific Board? What sort of input do they have?
- What is their grant review process?
- What is your funding strategy to foster drug discovery? Where are the bulk of your funds coming from currently to coordinate drug discovery?
- At what point in the drug discovery process do you engage with PIs, how much $ do you provide them, and what sort of support/resources do you offer?
- How do you see the current performance of drug discovery in your university?
- How do you streamline drug discovery process within your university?

- What is your organizational structure to foster drug discovery? What other groups within the university do you work with?
- What type of internal resources do PIs utilize? What works well, and what doesn't?
- How do you develop a culture of drug discovery/development amongst PIs at your institution? What sort of educational material do you offer them?
- Do you have an internal marketing strategy to develop awareness of your center?
- How do you develop partnerships with industry? What is your strategy and marketing?
- What is you metric of success in terms of drug discovery?
- What are the milestones, if any, that you utilize to measure progress during the discovery process for PIs?

Questions for OTT (other universities)

- What is the typical workflow of OTT with drug discovery process? What's working and what's not?
- How do you see the current performance of drug discovery process in your university? What's working and what's not?
- How much licensing revenue comes from drug discovery each year? What is your strategy to effectively increase licensing revenue?
- When do you start work with PIs in the course of drug discovery?
- When is the best timing to start working with OTT?
- Who within drug discovery community in your university do you work with in the course of your evaluation?
- How many proposals do you typically see in this area? What has trend been on that number, if any?
- What proportion of total evaluations are about drug discovery?
- What resources or information would better help you during the evaluation?
- What is the royalty distribution policy in your university? How is it determined?

Questions for VCs

- What is your strategy with therapeutics? Therapeutic area of emphasis?
- What is your strategy with regard to academic drug discovery?
- What metric do you use to evaluate academic drug discovery?
- What milestone do you use to make a deal?
- When do you typically start working with PIs?
- What is the best timing for PIs to start working with you?
- What are the major obstacles from VC point of view to make a deal with ADDC?
- How much funding do you typically provide (depending on stage of involvement)?
- More interested in funding Biotech/Biologics vs. Pharma/Small Molecule? How does the funding differ, depending on what area?

Questions for Pharma/Biotech

- What type of partnership have you made with ADDCs?
- What is your strategy to develop partnership with ADDCs? What is your incentive to build partnership? Could you give us some examples?

- How do you evaluate ADDC? What metrics do you use?
- What tools/avenues do you utilize to learn more about what universities are currently studying/developing?
- Where in the drug development process do you usually look to engage with academic centers (for licensing purposes)?
- How do you evaluate which academic drug discovery centers to invest/support with R&D funding? What does that relationship look like? Do they work with your personal/industry scientists, or are you more of a funding support?
- What are the major obstacles from Pharma/Biotech point of view to build partnership with ADDC?
- What do you think of potential to build partnership with U of M?

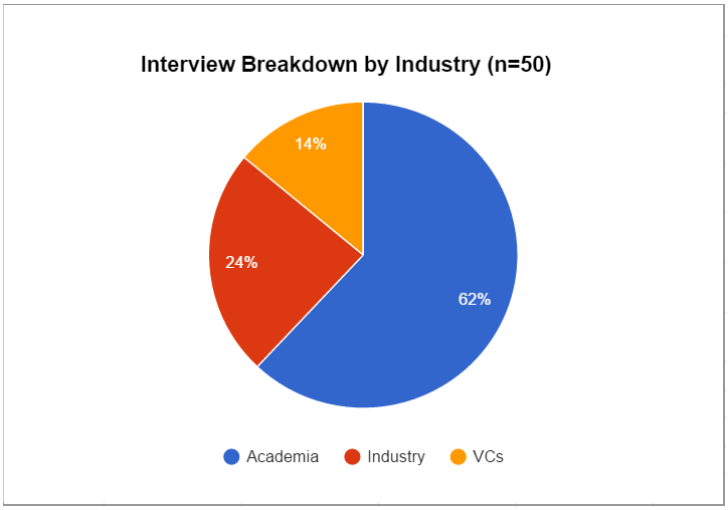
APPENDIX D – List of Interviewees

Interviews Completed

No.	Contact Name	Affiliation	Title / Department	Category	Connection Made Via
1	Jim Shayman	University of Michigan	Nephrologist and Inventor of Cerdelga	Academia	CDNM / LSI
2	Max Wicha	University of Michigan	Director, Comprehensive Cancer Center	Academia	CDNM / LSI
3	Aaron Westfall	University of Michigan	Business Development, LSI	Academia	CDNM / LSI
4	Laura Williams	University of Michigan	Business Development, LSI	Academia	CDNM / LSI
5	Ian Dempsky	University of Michigan	Marketing/Communications, LSI	Academia	CDNM / LSI
6	Robin Rasor	University of Michigan	Managing Director of Licensing, Office of Tech Transfer	Academia	CDNM / LSI
7	Jack Minor	University of Michigan	Director of Venture Center, Office of Tech Transfer	Academia	CDNM / LSI
8	Ann Schork	University of Michigan	Managing Director, LSI	Academia	CDNM / LSI
9	Eric Fearon	University of Michigan	Chief of the Division of Molecular Medicine & Genetics	Academia	CDNM / LSI
10	Ed Pagani	University of Michigan	Senior Licensing Specialist, Office of Tech Transfer	Academia	CDNM / LSI
11	Connie Chang	University of Michigan	Managing Director, Fast Forward Medical Innovation	Academia	CDNM / LSI
12	Tom Shanley	University of Michigan	Director, Michigan Institute for Clinical and Health Research	Academia	CDNM / LSI
13	Shaomeng Wang	University of Michigan	Research Scientist and Director, Cancer Drug Discovery Program	Academia	CDNM / LSI
14	John Tesmer	University of Michigan	Research Scientist, LSI	Academia	CDNM / LSI
15	James Dalton	University of Michigan	Dean, College of Pharmacy	Academia	CDNM / LSI
16	Lori Isom	University of Michigan	Interim Chair, College of Pharmacology	Academia	CDNM / LSI
17	Jeanne Stuckey	University of Michigan	Head of SAR Core	Academia	CDNM / LSI
18	Maggie Herron	University of Michigan	Research Process Coordinator and Finance Manager, LSI	Academia	CDNM / LSI

19	Martha Larsen	University of Michigan	Director of HTS Core, LSI	Academia	CDNM / LSI
20	Scott Larsen	University of Michigan	Director of Vahlteich Medicinal Chemistry Core, College of Pharmacy	Academia	CDNM / LSI
21	Duxin Sun	University of Michigan	Director of PK Core, College of Pharmacy	Academia	CDNM / LSI
22	Rajesh Ranganathan	NIH (NINDS)	Director of NINDS, NIH	Academia	CDNM / LSI
23	Stephen Frye	University of North Carolina	Director, Center for Integrative Chemical Biology and Drug Discovery	Academia	MAP Team
24	David Walt	Tufts University	Director, Tufts Institute for Innovation	Academia	CDNM / LSI
25	Curtis Keith	Harvard Blavatnik Biomedical Accelerator	Chief Scientific Officer, Office of Technology Development	Academia	MAP Team
26	Su Chiang	Harvard Blavatnik Biomedical Accelerator	Senior Associate Director	Academia	MAP Team
27	Issi Rozen	Broad Institute	Senior Director, Strategic Alliances	Academia	MAP Team
28	June Lee	University of California - San Francisco	Director, Early Translational Research: Translational Science Institute	Academia	CDNM / LSI
29	Mike Walters	University of Minnesota	Director, Lead and Probe Discovery Core, Institute for Therapeutics Discovery & Development	Academia	MAP Team
30	Elizabeth Ponder	Stanford University (ChEM-H)	Associate Director	Academia	MAP Team
31	Kevin Grimes	Stanford University (SPARK)	Co-Director	Academia	MAP Team
32	Donna See	Allied Minds	Vice President, University Relations	VC	CDNM / LSI
33	Doug Cole	Flagship Ventures	Managing Partner	VC	CDNM / LSI
34	Michael Gladstone	Atlas Ventures	Principal	VC	MAP Team
35	Larry Lasky	The Column Group	Partner	VC	CDNM / LSI
36	Dan Estes	Frazier Healthcare	General Manager	VC	CDNM / LSI

37	Kristina Burrow	ARCH Venture Partners	Managing Director	VC	CDNM / LSI
38	Anthony Philippakis	Google Ventures	Partner	VC	MAP Team
39	*Several Contacts*	Apjohn Group		Industry	CDNM / LSI
40	John Freshley	ONL Therapeutics	President and CEO	Industry	MAP Team
41	Sridar Natesan	Sanofi	Head of R&D, External & Academic Alliances	Industry	CDNM / LSI
42	Adam Keeney	Sanofi	Head of R&D, External & Academic Alliances	Industry	MAP Team
43	Morrie Birnbaum	Pfizer	CSO, Cambridge CTI	Industry	CDNM / LSI
44	Kiran Reddy	Biogen	Senior Director, Corporate Strategy	Industry	CDNM / LSI
45	Scott Lewis	Biogen	Senior Director, Corporate Strategy	Industry	MAP Team
46	Rose Loughlin	Biogen	Senior Manager, Business Development	Industry	MAP Team
47	Ann Schlesinger	Novartis	Industry-Academia Liaison, Novartis Institutes for Biomedical Research	Industry	CDNM / LSI
48	Ron Newbold	Pfizer	Head, Strategic Research Partnerships within External R&D Innovation	Industry	MAP Team
49	Maude Tessier	Merck	Director, Business Development at Cambridge Innovation Center	Industry	MAP Team
50	Gus Gustavson	J&J Innovation Center	Vice President, CVM Innovation	Industry	CDNM / LSI



APPENDIX E – ADDC Survey Questions

Thank you for participating in this survey about Academic Drug Discovery! This survey is being conducted by a team of University of Michigan Ross School of Business MBA students. We are performing this survey as a part of our Multidisciplinary Action Project, where we are developing a strategic plan for the Center for Discovery of New Medicines. All information you provide will be confidential. Results will be presented in an aggregate form in our final presentation and report to the Center for Discovery of New Medicines. If you would like a copy of the aggregated survey results, there will be an option for you to make this request at the end of the survey.

You may skip any question you prefer not to answer. If you are unable to complete the survey, you may resume where you left off by clicking the survey link in the invitation email. We estimate that this survey will take 15 minutes to complete.

For additional questions, please contact us at map15.171@umich.edu. Please click the button below to begin the survey. Thanks!

1. What is the official name of your Academic Drug Discovery / Center?
2. When was your Center founded? Please enter year only in (YYYY) / format.
3. How many tenure track faculty members receive services from your / Drug Discovery Center each year?
4. What percentage of the total financial support for your Center / comes from the following sources?
    a. Federal grants/contracts
    b. For-profit commercial organzations
    c. Charties/non-profits
    d. Private donors
    e. Your university/academic unit
    f. Revenue from IP generated by your center
    g. Disease advocacy groups or foundations
    h. Fee for services
    i. If other, please specify
5. What is the approximate total annual operating expense for your center (i.e., overhead and administrative expenses, such as salaries, equipment, supplies, etc.)? Please enter an integer
6. What is the approximate total annual budget for your center (i.e. funding for drug discovery projects)? Please enter an integer only
7. Over the next five / years, do you expect your funding to:
    a. Grow
    b. Stay the same
    c. Shrink
8. Does your center have any long-term exclusive or semi-exclusive relationship with a for-profit commercial partner?
9. Please describe your relationship(s) with these for-profit commercial partner(s).
10. With which areas of the drug discovery and development process does your Center support tenured faculty?
    a. target identification (genetic, si-RNA, pharmacology, etc.)
    b. in vitro or cell-based primary assay development
    c. high-throughput screening for hit generation (screens of >100K compounds)
    d. structure based drug design
    e. medicinal chemistry
    f. metabolism & pharmacokinetics (dmpk) measurements
    g. pre-clinical safety
    h. clinical trials
    i. patent filing / licensing / spin-offs
    j. overall project management
    k. other (please specify)
11. Are there other entities at your University that support drug discovery and development process? If yes, please list other entities that support drug discovery/development and what area in the process.
12. Which broad therapeutic areas are supported in your center? Please check all that apply.
    a. cancer
    b. diabetes, obesity, or metabolic disorders
    c. psychiatric or neurologic disorders

   d. cardiovascular disease
   e. infectious disease
   f. women's health
   g. dermatological disorders
   h. ophthalmology
   i. diseases of less developed countries
   j. orphan diseases
   k. other, please specify

13. What percentage of funding is currently allocated to each therapeutic area (checked in previous question)?
14. Which therapeutic approaches are supported in your center? Please check all that apply.
   a. small molecule
   b. antibodies
   c. other biologics (e.g., nucleic acids, peptides, etc.)
   d. vaccines
   e. regenerative medicine (e.g., stem cells, tissues, etc.)
   f. device
   g. other, please specify
15. What percentage of funding is currently allocated to each therapeutic approach (checked in previous question)?
16. How many targets have progressed to the following drug discovery stages at your Center? Please enter number of targets in each stage for target based and phenotypic assays. Integers only.
   a. target identification (genetic, si-RNA, pharmacology, etc.)
   b. assay development
   c. high-throughput screening
   d. structure based drug design
   e. medicinal chemistry
   f. metabolism & pharmacokinetics (dmpk) measurements
   g. in vivo pharmacology
   h. pre-clinical safety
   i. clinical trials
   j. patent filing
   k. licensing / spin-offs
17. Which of the following are an important part of the mission of your / Drug Discovery Center? Please check all that apply.
   a. training of graduate students and/or postdoctorals
   b. advancement of science through publications
   c. creation of intellectual property
   d. development of revenue streams for your institution
   e. progression of agents to clinical testing
   f. creation of new companies and/or local job creation/economic development
   g. addressing neglected patient populations
   h. lowering the cost of new therapeutics
   i. other, please specify
18. Please rank the importance of your previous selection (only populated selected items).
19. What is the major reason your institution created a Drug Discovery Center?
20. What are the major obstacles to maximizing the impact of your Center?
21. What question did we fail to ask that you think is important and / why?
22. If you would like an aggregated summary of this survey's results, / please insert your contact information below. Thank you!

APPENDIX F – University of Michigan PI Survey

Thank you for participating in this survey about translational research at University of Michigan! We would like your opinion on translational research at the university in order to inform the vision of the Center for Discovery of New Medicines.

This survey is being conducted by a team of University of Michigan Ross School of Business MBA students. We are performing this survey as a part of our Multidisciplinary Action Project, where we are developing a strategic plan for the Center for Discovery of New Medicines. All information you provide will be confidential. Results will be presented in an aggregate form in our final presentation and report.

You may skip any question you prefer not to answer. If you are unable to complete the survey, you may resume where you left off by clicking the survey link in the invitation email. We estimate that this survey will take 5 minutes to complete.

Please click the button below to begin the survey. If you have questions or additional feedback, please contact map15.171@umich.edu. Thanks!

1. Name (optional)
2. Email (optional)
3. What is your title?
    a. Chair of Department
    b. Professor
    c. Associate Professor
    d. Assistant Professor
    e. Research Investigator
    f. Postdoctoral Fellow
    g. PhD Student
    h. Other, please specify:

4. What University of Michigan Department are you in? Please select all that apply.
    a. Biological Chemistry
    b. Biomedical Engineering
    c. Cancer Center
    d. Cardiovascular Center
    e. Cell and Developmental Biology
    f. Computational Medicine and Bioinformatics
    g. Human Genetics
    h. Internal Medicine
    i. Learning Health Sciences
    j. LS&A
    k. Microbiology and Immunology
    l. Molecular and Integrative Physiology
    m. Pathology
    n. Pharmacology
    o. Pharmacy
    p. Other, please specify:
5. In 2014, what percent of time did your lab engage in the following activities? Please allocate 100 points across the following categories:
    a. training of graduate students and/or postdoctoral students
    b. basic research to advance biomedical knowledge base
    c. translational research to move agents into clinical testing
    d. advancement of science through publications
    e. seeking grants and/or funding for research
    f. other, please specify:
6. Which therapeutic areas does your lab perform translational research? Check all that apply.
    a. cancer
    b. diabetes, obesity, or metabolic disorders
    c. psychiatric disorders
    d. neurologic disorders
    e. cardiovascular disease
    f. infectious disease

g. women's health
h. dermatological disorders
i. ophthalmology
j. diseases of less developed countries
k. orphan diseases
l. other, please specify:

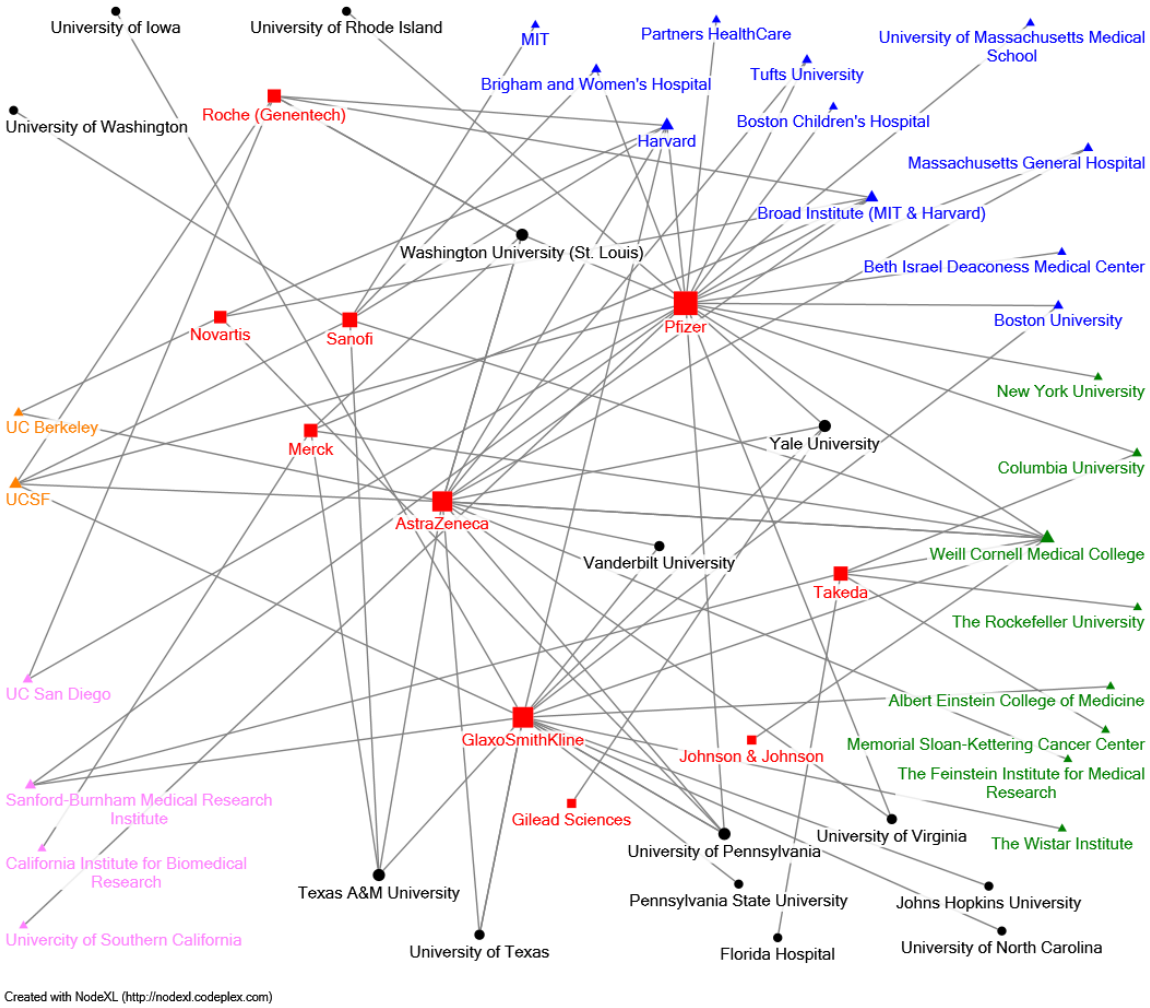
7. Which therapeutic approaches does your lab explore for translational research? Check all that apply.
   a. small molecule
   b. antibodies
   c. other biologic (e.g., nucleic acids, peptides, etc.)
   d. vaccines
   e. regenerative medicine (e.g., stem cells, tissues, etc.)
   f. device
   g. other, please specify

8. What are the primary obstacle(s), if any, to expanding drug discovery at University of Michigan?
9. Please indicate your familiarity with the following University of Michigan drug discovery programs (I am not familiar with this program, I have heard of this program, but I have not attended their events, I have engaged with this program by attending their events, I am an active participant in this program
   a. Center for Discovery of New Medicines (CDNM)
   b. Fast Forward Medical Innovation (FFMI)
   c. Michigan Institute for Clinical and Health Research (MICHR)
   d. Coulter Translational Program
   e. Translational Oncology Program
   f. Office of Technology Transfer
   g. Other, please specify:

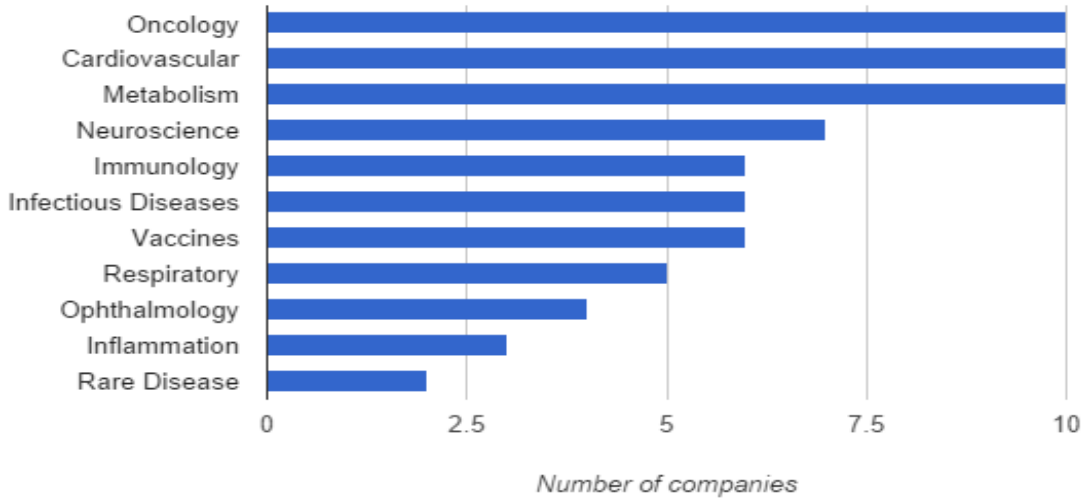
10. Please rank the following services in terms of importance to fostering drug discovery at University of Michigan. Drag and drop the items below to rank the items, with the top item being the most important.
   a. education and training programs about drug discovery
   b. progression of agents through clinical testing
   c. advancement of science through publications
   d. consultative services to researchers on how to move their compound to the next stage
   e. creation of new companies and/or job creation/economic development
   f. opportunities for funding
   g. connections to industry partners
   h. other, please specify:

11. What question did we fail to ask that you think is important to drug discovery at University of Michigan?
12. Do you think more translational funding should be available at University of Michigan?
13. How would you allocate additional funding for translational research at University of Michigan?
   a. Your Department
   b. Interdisciplinary Center (e.g., Center for Discovery of New Medicines, Fast Forward Medical Innovation)
   c. Core Lab Facilities (e.g., HTS, Structural Biology, Medicinal Chemistry, PK)
   d. Office of Tech Transfer
   e. Other

APPENDIX G – Network Map of Academic-Industry Collaborations



APPENDIX G – Therapeutics areas of focus for top 10 biopharma companies by total global revenue



APPENDIX H – Additional ADDC Case Studies

Vanderbilt Center for Neuroscience Drug Discovery

Background: Established in 2003 as part of the Department of Pharmacology, the center began as a means for the director, formerly a Merck neuroscientist, to pursue a novel target and compounds for schizophrenia. The Vanderbilt Center for Neuroscience Drug Discovery has now morphed into an institute with 100 scientists and four core labs (medicinal chemistry, PK, molecular pharmacology, and behavioral pharmacology)[56]. The promising nature of the target and compounds has yielded substantial federal grants and partnerships with AstraZeneca, Bristol Myers Squibb, and J&J, along with support from disease foundations.

Sole Focus: Vanderbilt's sole focus is small molecule therapies for neurologic disorders. This top-down approach, along with a focus on a small group of projects, has helped the center grow. The momentum built from the early success of the compounds that was the basis for the center's creation has resulted in a budget of $15 million. Although Vanderbilt does not operate a program for PIs outside of the center, it has been awarded a grant for a postdoctoral training program by the National Institute for Mental Health (NIMH), which will expose postdoctoral students to the lead optimization process.

Key Takeaway: Vanderbilt's narrow focus, combined with the preclinical success of the original novel target and compounds, has resulted in strong support from the government, especially the NIMH, along with attention from pharma and disease advocacy groups. Moreover, though the center started small, it began with support from university leadership from the very beginning[57], helping it establish stability before the grants came in. A combination of university support, narrowly focused projects, and "bench-to-bedside" emphasis has contributed to its funding success.

University of North Carolina Center for Integrative Chemical Biology and Drug Discovery

Background: Established in 2007 as part of the School of Pharmacy, the Center for Integrative Chemical Biology and Drug Discovery's focus is small molecule oncology therapeutics and chromatin regulation. It began in conjunction with the School of Pharmacy, Cancer Center, School of Medicine, and Department of Chemistry. The center has capabilities in assay development, compound screening, medicinal chemistry, and computational chemistry (structure based drug design)[58], while PK activity is outsourced to CROs. The center does not engage in fee-for-service activities or partner with industry, instead focusing on collaboration with PIs and other university centers, namely the Center for Nanotechnology in Drug Delivery and the Institute for Pharmacogenomics and Individualized Therapy. It is funded by federal and state grants, the university, and a recent alumni donation of $3 million.[59]

Core Services Integration: The center collaborates with PIs after evaluating their proposals based on description of the target and assay development, funding status and outlook, and alignment with center's project portfolio. Once a proposal has been accepted, a formal project plan is created, outlining the extent of the center's capabilities to be utilized over the course of the project[60]. The center's director and core lab directors then work with the PIs as collaborators on projects, often jointly submitting grants to move projects forward. There is a scientific advisory board that helps assess the center's portfolio and project process, but no specific project management is in place for each project. The combination of the center's capabilities and operations has resulted in $22 million follow-on grant funding over the past 8 years, with the center collaborating on 5-6 projects with PIs every year.

Key Takeaway: The key selling point of the center is its' core capabilities and focus on project collaboration (without a fee-for-service component). Although it does not operating as a seed funding program or provide formal educational support, the relationship that the core labs have with PIs on project progress, publishing, and grants has resulted in the center's success in receiving continued grant funding.

Stanford Chemistry, Engineering & Medicine for Human Health (ChEM-H)

Background: Established in 2014 as a nexus for interdisciplinary research, spanning biology, chemistry, medicine, and engineering for promotion of human health, the center, funded by the university, currently provides $50,000 in seed funding to projects that require interdisciplinary PI involvement. ChEM-H has also established "knowledge centers" for medicinal chemistry and structural biology (still in pilot phase) which have an expert in each core function who are set up to be consultants and collaborators. The center pays for 20% of the salary for these experts to act in a consulting capacity for ChEM-H projects, which is separate from the direct work that the experts do beyond on a project itself.

Education Component: A key aspect of ChEM-H is its emphasis on education and collaboration. ChEM-H faculty fellows mentor postdoctoral students and spearhead events, while students have created a ChEM-H Postdoctoral Society, where postdocs create a

community, interact with ChEM-H leadership, and gain advice from faculty. Novartis and ChEM-H also collaborate on an educational program meant to bridge understanding between industry and academia[61]. Components of the collaboration include a case-based simulation course, teaching PIs from different disciplines to understand each other and drug discovery, informal networking sessions, a seminar series involving academics and industry, and an agreement in which Stanford chemistry PhD candidates are eligible for an internship before starting their studies.

Key Takeaway: ChEM-H emphasizes creating a collaborative community within the university, with education a critical component. Bridging gaps in translational research knowledge, between disciplines, and gaps between investigators drive the seed funding requirements, collaboration with Novartis, and faculty mentoring. ChEM-H is another example that highlights not only the need, but also the interest in learning, training, and relationship building within an ADDC community.

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