INVO Innovation and New Ventures Office

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Innovation Corps: A review of a New National Science Foundation Program to Leverage Research Investments

Thank you Chairman Brooks, and Ranking Member Lipinski, for the opportunity to testify today. Northwestern University and I appreciate your interest and support for science and technology issues. My name is Andrew Mazar, Director of the Center for Developmental Therapeutics and Entrepreneur-in residence. My research interests focus on mechanisms of cancer metastasis and progression and the development of new cancer drugs. Today, I am representing the perspective of an Entrepreneur-in-Residence, or EIR. Northwestern created this position to address the unique challenges encountered when advancing novel therapeutic projects through development in the academic setting. The traditional description of an EIR is a senior levels leader who has founded and run a start-up company successfully and is looking for that next opportunity. This EIR generally sits within a venture investment firm and oversees the development of a particular project to some pre-defined milestone, at which point the EIR and technology are spun-out into a stand-alone start-up company concomitant with a funding commitment from the venture firm and possibly a syndicate of co-investors. Although certain aspects of this vision have been built into our vision of the university EIR, there are a number of unique attributes that make the phenotype of this position align closely with the academic mission.

Northwestern first created the EIR position within the Chemistry of Life Processes Institute (CLP). CLP is an "institute without walls" that provides the infrastructure necessary to help articulate and explore emerging research questions across the disciplines of physics, chemistry, biology, engineering, medicine, and computational science. The Institute acts as an umbrella for a variety of centers, facilitates collaborations and helps bridge these different cultures. The Institute draws its membership from thirty-six faculty members in four schools within Northwestern University and integrates the activity of more specialized Centers on campus.

The Chemistry of Life Processes Institute at Northwestern provides a robust ecosystem for basic and translational research that transcends disciplinary boundaries. This ecosystem is built upon a custom designed physical environment for transdisciplinary research in the Richard and Barbara Silverman Hall for Molecular Therapeutics and Diagnostics, which functions as a nexus for interaction and collaboration between the physical, engineering and life science researchers. Seven state-of-the-art core research facilities devoted to various areas of therapeutic and diagnostic development are based in Silverman Hall, and there is also space for future expansion.

A critical component of this ecosystem is the capacity to move discoveries from the laboratory bench into the hands of society. The Institute provides researchers with the tools needed to translate their discoveries through the EIR program to bridge academic and commercial environments, and works in tandem with Northwestern's Innovation and New Ventures Office (INVO). As the EIR, I partner and collaborate on many different projects with faculty members across all the different Northwestern schools. In doing so, we have formalized a Northwestern therapeutics pipeline; currently, there are more than 30 projects active in this pipeline. I bring something different to each project depending on that project's needs: in some cases, I take a hands-on role as a collaborator and co-investigator to carry out certain studies needed to develop a new therapeutic. In other cases, I provide advice and mentorship or facilitate connections to colleagues in the pharmaceutical and biotechnology space or to investors. In fact, several non-Northwestern faculty have also sought my collaboration in setting up new start-ups and helping develop their therapeutic projects to the clinic. I have now helped found seven companies (Tactic Pharma, Valence Therapeutics, Modulytics, Vascular Solutions, Inc., Lung Therapeutics, Inc. (LTI), Remedyon, Zephyrus) in the past two and one half years since assuming my role as EIR. I have also founded a Center for Developmental Therapeutics at Northwestern that I now direct, which provides hands-on assistance with the development of new therapeutic projects. I have helped obtain a NCI NExT award for a Tactic Pharma project; a SMARTT award for a LTI; seed capital from the Horizon Fund at the University of Texas for LTI; and a venture investment from HealthCap Ventures into another Tactic project that was spun out into a new company called Wilson Therapeutics AB. I have ongoing discussions with a pharmaceutical company who is interested in partnering on a different Tactic project as well as angel investors who want to provide seed funding to Remedyon and Zephyrus. I have also directly assisted several of these start-up companies prepare STTR/SBIR application (Modulytics, Valence, Vascular Solutions). Thus, I think we are demonstrating that we can bridge the academic-commercial divide and build value by advancing therapeutic projects further than was historically done in the academic setting given the proper culture and support that allows these types of activities to thrive.

This environment also nurtures the next wave of transdisciplinary researchers through multiple training and fellowship mechanisms that build upon the unique aspects of the CLP research programs and facilities. The Institute provides a robust training program for undergraduates, graduate students, and postdoctoral fellows in transdisciplinary biomedical research, including summer and academic year laboratory research programs that provide NU undergrads with their first experience in cross-disciplinary research. The Institute also developed a unique postdoctoral fellowship program that fosters highly collaborative, transdisciplinary research and entrepreneurial training to foster the development of independent scientists that possess the skills needed to address the "big questions" facing biomedical researchers in the 21st century.

My EIR position was the first of its kind created at Northwestern, although there have been additional EIR positions created across the university since then. The position was created as part of a new model of interdisciplinary collaboration to bring new perspectives to solving unmet medical needs. We recognized that in order to do this successfully, we would need to facilitate moving these ideas toward commercialization. The development of new therapeutics requires enormous resources, and, therefore, by definition, CLP had to be "outward facing." The EIR had to be someone that had both an academic as well as a therapeutics commercialization pedigree and could work at this interface and facilitate a flow of projects from the university to the outside community. In addition, in conjunction with the creation of the EIR, Northwestern revamped its technology transfer office, now known as the Innovation and New Venture Office, or INVO, to encourage greater collaborations and synergies between the CLP EIR and the INVO team. I work very closely with the INVO team and try to help them build value to projects that they then partner. I also identify projects with a therapeutic focus before INVO sees them (what we refer to as pre-IP or before an invention disclosure if submitted) and try to not only get these projects on the INVO radar but also help guide how they are developed early on with an eye towards putting together the strongest IP protection possible.

I believe that the collaborative interaction that I enjoy with INVO has also been spurred on by the success of Lyrica, which is a drug marketed by Pfizer that was invented at Northwestern. Lyrica is a tremendous example of leveraging the federal investment in basic research to develop a new drug that is benefiting millions of people (societal benefit) as well as generating a revenue stream for Northwestern that is being re-invested to create new programs. In fact, the inventor of Lyrica, Professor Richard Silverman, made Silverman Hall possible through a generous donation of a portion of his Lyrica proceeds and he is part of the CLP faculty. This type of royalty stream and re-investment by the university is especially important in today's challenging funding environment as it provides an alternative source of capital that can be used to build transformative and disruptive programs in the academic setting such as CLP and the EIR, something that is not always possible through traditional grant mechanisms. Further, I believe that the success of Lyrica has bolstered what was already a very entrepreneurial culture in some of the Northwestern Colleges and taken it mainstream across the entire campus. The number of people thinking about their research in terms of translation and commercialization has grown exponentially since the EIR was put in place and I think has helped inform a revamping of the approach that the university now takes to technology transfer.

Historically, tech transfer has been very passive, i.e. someone from the outside community sees a project they are interested in, or a faculty member that they want to work with, and that is how a relationship is forged. This approach can prove challenging for individuals in the community to really understand the technologies that a university has available for license, their stage of development, and therefore their valuation. Northwestern's approach to encourage collaboration between the EIR and INVO has made the university much more proactive. We now try to build value to projects before they are partnered by finding ways to advance them in the academic setting (i.e. through the centers and cores of CLP). We identify and get involved in projects earlier so we can improve how they are developed and protected (this comes out of my expertise in discovering, developing and taking into the clinic a number of drugs, a skill set which is not typically found in academia). In this way, we prepare better patents and can be more selective in making the investment in IP. We now also work with faculty to form and nurture start-up companies and take an active role in this process, marketing projects proactively instead of just waiting for people to come to us. Our faculty benefit from this because they now have mentorship in commercialization and people that they can go to for help. Hopefully, this will lead to an increase in the

number of projects being partnered or spun-out. For the first-time entrepreneur, these are tremendous benefits and form a nurturing entrepreneurial community. In turn, this allows the university to recruit better faculty with these same attributes.

Let me now speak to the challenges. One of my biggest challenges is human resources. As more people become interested in working with me on translating their ideas to the clinic, my capacity has been constrained. My biggest fear is that people will lose interest or fall through the cracks if I am unable to connect with them quickly. Historically, faculty have been wary of tech transfer offices because they felt that they were not responsive to their needs, thus both my office and INVO have made tremendous efforts to be responsive and meet with people to get them into the pipeline.

A second challenge has been to overcome the perception that discovering and developing new drugs or diagnostics is not part of the university mission or that somehow this type of scientific pursuit is inferior to more basic knowledge-generating research. I believe that academic drug discovery and development is one of academia's most important missions. Drug development creates new knowledge and technology for every new product that is developed. Drug development is inherently cross-disciplinary and creates new models for collaborative research across departments and schools internally, as well as externally with other institutions. Contrary to popular belief, most studies performed as part of a drug development project (e.g. animal model studies) are published, consistent with maintaining academic freedom. Further, drug discovery and development is highly entrepreneurial (one creates something that did not exist before) and is therefore consistent with the entrepreneurial nature to which most universities aspire. Finally, commercialization of new therapeutics helps the US grow its economy and maintains its global competitiveness. Again, this is aligned with the mission of a university.

The last major challenge that I would like to comment on is funding. I believe that it is possible to discover and develop new drugs through early proof-of-concept studies in the academic setting and that large research-driven institutions with medical schools such as Northwestern could become quite good at this if funding was available. Today, we do not have a fund that can provide the capital required for these types of activities. Thus, I have to access grants and development resources at NIH and DoD that can pay for pre-clinical development that will support an Investigational New Drug (IND) application. This requires that I be a co-investigator or principle investigator on these applications and drive their preparation and submission. This takes time away from my other activities and, unfortunately, there are not enough of these programs available and the application process is slow. Other academic institutions have been able to raise small gap funds, usually through philanthropy, but in most cases these have not provided adequate resources to really move projects forward. There are some examples (Michigan, Harvard) of gap funds that were allowed to invest sufficient capital in promising projects, and returns on investment have already been observed just a few years after the initial investment. Utilized properly, a gap-funding model can support drug discovery and development. In addition, by making these funds self-sustaining (or "evergreen"), an initial investment can provide a capital base that potentially generates a program capable of perpetual funding.

One way that government could accelerate commercialization of academic technologies (and I believe that this is in keeping with the mission of the I-Corps program) such as new drug and diagnostics, would be to invest in these gap funds regionally, so that non-grant capital that can be put to work rapidly would be available to support commercialization activities such as drug development. Currently, it may take me several years to go through the grant application process to secure support on a project by project

basis. For example, I mentioned the SMARTT award on which I am a Co-PI. The implementation, application and subsequent start of that program was something that took several years to get into place. If I had access to gap funding, I could have had that project to the end of a phase I trial in the time it took to secure that award. Patients would have already had access to a new drug and if it showed signs of clinical activity, the university could have already realized a return on this project. The caveat is that at least $2-3M would have had to be committed to that project and the tendency with many existing gap funds is to put in small amounts of money into many projects. I think there is still room for that kind of support but there also has to be sufficient capital to make a few large bets each year because these will be the value drivers for potential pharma partnerships, investments, and returns in the near term.

I believe that the EIR program can be replicated at other institutions if their culture is open to new models of academic entrepreneurship. There are many flavors of possible EIRs (traditional venture EIR, my EIR model at NU, others in between) and these could be molded to fit the specific needs of each institution. One idea would be to create a national academic EIR program. It would be even more interesting if that program could also provide a gap fund for each EIR. This gap fund could be provided locally for each EIR, or there could be a central gap fund to which all the EIRs could have access. Projects would be selected for funding competitively through an independent external review committee and each EIR could champion his/her institutions own programs for this funding. In some ways, this is the model that is being advanced through the National Heart, Lung and Blood Institute (NHLBI) Centers for Accelerated Innovation (CAI) (RFA-HL-13-008). Thus, the beginnings of a national entrepreneurial ecosystem are starting to form and this should be nurtured and developed.

Historically, good researchers have not been considered to be good business people and venture backed start-ups developing drugs rarely had a scientist CEO. However, this is now changing in the drug development space. When an IPO was the preferred exit strategy, selling the story was most important and traditional CEO's with a business background were the logical choice to lead these efforts. Now, the exit strategy is to find a pharma partner to either license or buy a new drug asset and thus, the metrics have changed. There now has to be very solid science and research behind each product, otherwise it will never survive the due diligence process. This has created an opportunity for scientist CEO/entrepreneurs to guide start-up companies and has created a need for mentoring and training these individuals. Most of Northwestern's entrepreneurship training has been geared toward students and not faculty. However, this is changing. Northwestern's Farley Center for Entrepreneurship and Innovation provides faculty support in entrepreneurial activities. The Levy Institute at the Kellogg Business School runs an Entrepreneurship and Innovation Program that is open to faculty. Northwestern, along with the University of Illinois at Chicago and the University of Chicago, have instituted the Chicago Innovation Mentor (CIM) program that forms mentorship teams to work with faculty inventors from all three schools to advance commercialization of their therapeutic, diagnostic and device ideas. iBio also has the Propel program that matches entrepreneur mentors with faculty interested in forming start-up companies. I also partner with individual faculty to mentor them in translation of new therapeutics, as described above, and I believe there will be more such programs launched in the future. For example, the CAI described above will have a training component to mentor faculty in translation and commercialization of new therapeutics, diagnostics and devices in areas of interest to the National Heart, Lung and Blood Institute (NHLBI). Additional programs like this funded through government agencies would also boost these activities.

Chicago is a very unique area in terms of commercializing new therapeutics. Despite the academic intellectual firepower, many early stage academic therapeutic projects with commercial potential, and several large pharmaceutical companies in the vicinity, there is a paucity of investment in biotechnology spin-out companies and not many larger venture firms that invest in that space are located in the area. When technologies are spun-out, they end up going somewhere else geographically. Not having a large group of venture investors in the area definitely hurts our ability to create spin-outs because investors just don't think about Chicago when they think about investing. Baxter has a program with Northwestern where they provide small grants for Northwestern early stage projects but these are typically small and insufficient to support translation. However, it is my understanding that Baxter would like to begin supporting projects with true translational potential in the future so this situation may change. Similarly, the Chicago Biomedical Consortium has also provided a lot of early stage basic science support and is also looking to move more into the translational space, another good sign for Northwestern and the Chicago area.

I believe that there is a real opportunity for the government to provide funding that would be truly disruptive and transformative by creating a national EIR program that comes with a gap fund, as described above, and could also encompass a hands-on training component for faculty. For example, faculty that submit a project that receives funding from the gap fund component of such a program could have the option to actually see their project through to some inflection such as a partnership with a pharmaceutical company or forming a spin-out company and closing on financing for that company. This type of funding could help transform the Chicago drug translation and entrepreneurial ecosystem, which is burgeoning, but needs the injection of funds to push it over the top. All the pieces are already here, we just need the resources to connect the dots. I believe that if federal funds were available, these could be leveraged through a variety of local sources to form private-public partnerships to support the types of entrepreneurial programs described above. This could replicated throughout the country.

I believe that I-Corp program is trying to do exactly this and should be expanded. My understanding is that there is concern that this is not a basic enough academic mission for the NSF to fund but I have provided some examples of how entrepreneurial activities are absolutely aligned with the basic mission of a university in terms of knowledge generation, economic growth, and contributing to the benefit of society. Without programs like I-Corp, the basic research investment will be wasted. If gap funding is not available and if venture capital is no longer investing in early stage projects, which it is not, then basic research sits on a shelf somewhere and all these marvelous basic discoveries never see the light of day. Or, someone sees that information in a publication in a country outside of the US, they invest in its development, and we lose the economic benefits of developing this technology ourselves. The most important thing that I would like to see from the I-Corps program is to make more funds available for each project. Each project should be evaluated for what milestone or inflection needs to be met next, and sufficient capital should be provided to support this. The milestones may be scientific, commercial or a combination of the two but providing insufficient funds is as bad as providing no funds at all. Given that there are limits on how much money is available for this program, I would favor making a few meaningful bets rather than trying to fund as many projects as possible and have none of them really move forward. This is not to say that the federal government should bear the cost of these types of programs alone. It is possible to leverage the federal investment with private funding and in fact, the federal investment can be viewed as a de-risking strategy that attracts private funding that would not otherwise be available. This is the strategy of the CAI program described above, which requires a commitment of non-federal dollars to leverage the federal investment. Another example of matching

public to private funds is the CIPRIT program in Texas, which will match on a 2 for 1 basis, funds obtained from private investors for start-up companies. The I-Corp program is already doing something like this by requiring identification of potential customers for each technology funded and I believe that if I-Corps funding is increased, this approach can be expanded to seek out actual commitments of funds that can match or exceed the government investment. This drastically lowers the barriers for entry into commercialization and in my opinion, spurs entrepreneurship and economic growth.

Mr. Chairman, thank you for providing me an opportunity to provide testimony at this field hearing on the Innovation Corps. This concludes my remarks. I would be happy to answer any questions that you may have at this time.