Repurposing Approved and Abandoned Drugs for the Treatment and Prevention of Cancer through Public–Private Partnership

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The cancer medical community, perhaps more than any other, understands the dire need for new, innovative therapies for the estimated 11.7 million Americans living with cancer (1). While our understanding of the biology and genetics of cancer has increased dramatically in recent decades, the pace of discovery, development, and registration of new drug therapies for the treatment, prevention, and control of cancer has not. This is especially true for the many rarer forms of cancer. Indeed, many cancers meet the Orphan Drug Act definition of <200,000 prevalence in the United States (2). Understanding cancer in this light and making meaningful inroads into the development of targeted therapies for these rare diseases requires new thinking, new approaches, and new collaborations.

On July 6, 2010, leaders from industry, government, academia, and nonprofit organizations participated in a national Town Hall co-sponsored by The University of Kansas Cancer Center (KUCC), the Ewing Marion Kauffman Foundation, the Kansas Bioscience Authority, the Friends of Cancer Research, and the Council for American Medical Innovation (CAMI). This Town Hall meeting, entitled "The New Role of Academia in Drug Discovery and Development," drew attention to academia’s changing role in translational research. Today, academic institutions are poised and challenged unlike ever before to meet society’s expectation that breakthrough technologies and bio-pharmaceutical industry in Bethesda, MD entitled "NIH-Industry partnerships key recommendations coming out of the event (3).

In January 2011, Secretary Sebelius further called for strategic partnerships between industry, government, academia, and nonprofit organizations to build "a stronger foundation for a new century of treatments and cures" (4). Responding to this challenge, three organizations with forward-thinking strategies and unique respective drug repurposing experiences established The Learning Collaborative to advance therapies for blood cancers more efficiently than any of the component organizations could do alone. This collaboration represents the future in cancer drug development—a team effort that brings together unparalleled strengths in the various disciplines needed to advance a treatment from the laboratory to regulatory approval as rapidly as possible. The Learning Collaborative is a dedicated collaboration between the NIH Chemical Genomics Center (NCGC) and its Therapeutics for Rare and Neglected Diseases (TRND) program, The Leukemia & Lymphoma Society (LLS), and KUCC to discover and develop new drug therapies for rare blood cancers. Specifically, The Learning Collaborative combines the disease expertise and network of the LLS, the cancer drug repurposing and drug development expertise of the KUCC, and the drug discovery expertise of the NCGC to create a pipeline of new therapies to treat blood cancers using less traditional forms of drug discovery and development. The partners have a shared commitment not only to discovering and developing new molecular entities (NME) for the treatment of rare blood cancers but also to exploring new uses for approved and abandoned drugs. The Learning Collaborative is advancing blood cancer–focused projects from target identification and validation through clinical proof-of-concept.

Repurposing Drugs for the Benefit of Patients

While The Learning Collaborative is focused on both NMEs and repurposing, this commentary emphasizes drug repurposing strategies for two reasons. First and foremost, repurposing approved and abandoned drugs for cancer represents an opportunity to rapidly advance to patients promising drug therapies by capitalizing on existing data and experience. The same holds true for abandoned or "shelved" drug candidates, agents whose development was discontinued for any number of non-safety–related reasons. NIH has taken notice of the important potential of repurposed and abandoned drugs (5). In April 2011, Dr. Francis Collins convened a meeting with research and development leaders from the pharmaceutical industry in Bethesda, MD entitled "NIH-Industry

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Roundtable—Exploring New Uses for Approved and Abandoned Therapeutics. A major objective of this meeting was to seek industry support in accessing approved and abandoned drugs for evaluation in patients suffering from rare and neglected diseases. Second, drug repurposing provides opportunities for The Learning Collaborative to interact with regulatory agencies, in accord with The Learning Collaborative’s objective of creating new and more rapid paths to regulatory approval of cancer drug therapies. Both provide critical learning opportunities and thus allow this nontraditional collaboration to evolve scientifically and operationally.

A New Academic Model

Drug discovery and development is universally acknowledged to be costly, time-consuming, and risky. Academia unfortunately faces additional barriers, deeply rooted in the conventional dynamics of university faculty, infrastructure, and process. The typical American academic institution is composed of research-oriented faculty who, in many cases, lack experience with the translational/regulatory process. Furthermore, even preeminent academic institutions are often deficient in core drug discovery and development functions, as traditional grant funding patterns and the tenure system incentivize basic research rather than translation. These circumstances make it difficult for academia to play a broader role in drug discovery and development. Success now requires charging forward with new, innovative approaches to the entire translational process. Indeed, the new National Center for Advancing Translational Sciences (NCATS) at NIH is envisioned as catalyzing just such technological and paradigmatic advances in the academic sector.

The Learning Collaborative

In June 2010, The Learning Collaborative’s three founding partners combined forces in an effort to bridge the “Valley of Death,” bringing together proven expertise in blood cancer research, drug discovery, and drug development. At the outset of this endeavor, founding partners established a Memorandum of Understanding to clearly define collective objectives, expectations, and deliverables. The partners designed these objectives and expectations to meet the new challenges of drug discovery and development. This partnership soon became a benchmark for innovation at NIH after becoming one of the first nonprofit/academic endeavors to receive a Cooperative Research and Development Agreement (CRADA) designation. Importantly, The Learning Collaborative obtained this CRADA designation because of the demonstrated capacity of the LLS and KUCC to develop and commercialize drug therapies as nonpro

Figure 1. The Learning Collaborative partner contribution across the drug discovery and development continuum. The logos contained within this figure are approved for usage.

The success of this rare public–private partnership is based on the fact that each participating organization offers unique, well-established capabilities. As the largest private disease philanthropy organization focused on blood cancer, LLS brings access to cutting-edge basic research. In addition, the LLS Therapy Acceleration Program, which supports projects focused on development of new therapies for blood cancer, has established partnerships with pharmaceutical and biotechnology companies that provide an avenue to license drug therapies developed by The Learning Collaborative to for-profit partners. NCGC and its TRND program established the first drug discovery and development pipeline within the NIH to produce new therapies specifically for rare diseases; The Learning Collaborative uses this organization’s ability to provide high-throughput screening and medicinal chemistry. KUCC provides cancer biology, drug discovery, early-stage drug development, and experimental therapeutics expertise as well as regulatory know-how to the collaboration. Through informed, structured planning and unprecedented industry collaborations, KUCC ensures that The Learning Collaborative’s core competencies in research are fully leveraged forward to commercial viability.

Auranofin for the Treatment of CLL

The Learning Collaborative’s first project, which is also a pilot project of the TRND program, focuses on repurposing an existing small-molecule drug, auranofin, initially approved to treat rheumatoid arthritis in the mid-1980s. The Hematology Branch of the National Heart, Lung and Blood Institute (NHLBI) at NIH is collaborating with The Learning Collaborative on this groundbreaking project. Auranofin is being evaluated by The Learning Collaborative as a treatment for relapsed chronic lymphocytic leukemia (CLL)—one of the four major types of leukemia and one that typically affects older people. Almost 15,000 people in the United States are diagnosed with CLL each year. Although current treatments for CLL are effective over the short term, patients frequently relapse and the disease remains incurable. The development of new, effective therapies is essential. In just 2 years after the identification of auranofin’s activity in CLL cells, this project has entered
Clinical trials. By conducting the experimental therapeutics trial at three institutions, KUCC, NHLBI, and The Ohio State University (Columbus, OH), patient enrollment will be accelerated. Upon clinical proof-of-concept, The Learning Collaborative will engage a for-profit partner to advance auranoif through late-stage drug development, registration, and commercialization.

The development of new therapies for blood cancers poses both scientific and economic challenges. The Learning Collaborative has the unique ability to "de-risk" promising drug therapies, such as auranoif, using an innovative approach to quickly determine proof-of-concept. This partnership represents a standing model for innovative practice and multi-stakeholder collaboration in drug discovery and development. The effort provides academia with opportunities to leverage funding, build organizational strengths, and clearly define exclusivity path(s) required to attract interested for-profit partners. Partnerships, such as The Learning Collaborative, are the key to addressing unmet medical need in this increasingly difficult landscape.

The partnership is named The Learning Collaborative because this model is scalable, applicable across a wide range of therapeutic areas, and replicable by organizations committed to innovative models of collaboration. Learnings from The Learning Collaborative will contribute to building a stronger foundation for translational research in America, leading to the advancement of new treatments for rare diseases, including rare cancers. In the past year, The Learning Collaborative surmounted many potential barriers and experienced important learning moments that positively steered the partnership. Some early successes that can be replicated include best practices in leveraging funding from multiple sources, integrating technology transfer into teams, and development of novel approaches to preclinical and clinical proof-of-concept. Members of The Learning Collaborative continue to explore solutions to barriers that include addressing regulatory science issues (with particular focus on repurposing off-patent and abandoned drugs for rare and neglected diseases) and defining exclusivity path(s) to interest future for-profit partners.

The Learning Collaborative is currently evaluating and selecting additional blood cancer drug discovery and development projects. Additional projects will use drug discovery and drug repurposing strategies. Projects are being identified on the basis of research conducted by the 3 collaborating organizations as well as research conducted by other academic institutions.

Engaging in Repurposing Partnerships

As shown by The Learning Collaborative, a new collaborative model of drug discovery and development can yield successful results. Each member of the collaboration posses individual assets that can be leveraged and integrated to advance promising drug therapies to patients. The foundation of a strong collaboration centers on a willingness to coalesce around the shared goal of translating discoveries from the laboratory to marketplace. In this new model, traditional practices may not be suitable, and collaborators may need to develop novel technology transfer, patenting, licensing, and funding streams.

Advances in Regulatory Science and Public Policy

To promote collaborative practices and their success, advancements in regulatory science are necessary. Priority areas include developing guidance on drug repurposing, increasing data-sharing and disclosure about drug development failures, modernizing regulatory pathways based on new science, and designing new exclusivity strategies. While these advancements would not be a cure all for the challenges of drug development, they are a strong step toward de-risking the process and promoting innovation.

A particular development challenge exists in repurposing off-patent drugs for rare cancers; regulatory approval often requires expensive and complex clinical trials, but limited returns on investment make it difficult to attract private sector financing and expertise. New paths to exclusivity and pricing/reimbursement strategies are needed to promote private sector engagement. In addition, it will be critical to create innovative public policy solutions that incentivize repurposing off-patent drugs for rare cancers—particularly, for small biotechnology companies, which may find opportunities in lower margin and small (but well-defined) markets attractive.

Conclusion

Nontraditional, dynamic partnerships, such as The Learning Collaborative, allow nonprofit organizations to play a high impact role in advancing the development of new cancer drug therapies and bringing these therapies rapidly to patients. The foundations of The Learning Collaborative model are a willingness to rely on partners for expertise, share freely, stay focused on the shared goal of translating discoveries from the laboratory to marketplace, and view deliverables as not only new treatments but also improvements in the processes by which those treatments are developed. The Learning Collaborative model allows the partner organizations to more effectively advance their missions to bring new therapies to the millions of patients suffering from rare cancers.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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References


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