

# DAY ONE PROJECT

## Repurposing Generic Drugs to Combat Cancer

Laura Kleiman  
Shruthi Bhimaraju

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## Summary

Cancer patients urgently need more effective treatments that are accessible to everyone. This year alone, an estimated 1.9 million people in the United States will receive new cancer diagnoses, and cancer will kill more than 600,000 Americans.<sup>1</sup> Yet there are no targeted therapeutics for many cancers, and the treatments that do exist can be prohibitively scarce or expensive.

Repurposing existing drugs, especially off-patent generics, is the fastest way to develop new treatments. Hundreds of non-cancer generic drugs have already been tested by researchers and physicians in preclinical and clinical studies for cancer, some up to Phase II trials, and show intriguing promise. But due to a market failure, there is a lack of funding for clinical trials that evaluate generic drugs. This means that there isn't conclusive evidence of the efficacy and safety of repurposed generics for treating cancer, and so cancer patients who desperately need more (and more affordable) treatment options are unable to realize the benefits that existing generics might offer.

To quickly and affordably improve the lives of cancer patients, the Biden-Harris Administration should create the Repurposing Generics Grant Program through the National Cancer Institute. This program would fund definitive clinical trials evaluating repurposed generic drugs for cancer. A key first step would be for President Biden to include this program in his FY2022 budget proposal. Congress could then authorize the program and related appropriations totaling \$100 million over 5 years.

## Challenge and Opportunity

### *Cause for Urgency*

Cancer takes an enormous toll on our society, healthcare systems, and economy. Following diagnosis, the lives of cancer patients and their loved ones are transformed overnight into a nightmare. Cancer is the second-leading cause of death in the United States, and the number of cancer cases is rising as the population grows, ages, and adopts lifestyle habits that increase risk for the disease.<sup>2</sup> By 2030, the number of cancer diagnoses in the United States is projected to increase by 45% relative to 2010,<sup>3</sup> rising from 1.6 million cases per year at baseline to 2.3 million cases per year in 2030. Costs are growing commensurately. Our nation now spends more than \$150 billion annually on cancer care.<sup>4</sup>

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<sup>1</sup> American Cancer Society. (2021). [Cancer Facts & Figures 2021](#).

<sup>2</sup> Cancer Research UK. (2021). [Causes of Cancer and Reducing Your Risk](#).

<sup>3</sup> Smith, B.D.; et al. (2009). [Future of Cancer Incidence in the United States: Burdens Upon an Aging, Changing Nation](#). *Journal of Clinical Oncology*, 27(17): 2758–2765.

<sup>4</sup> National Cancer Institute. (2020). [Financial Burden of Cancer Care](#). *Cancer Trends Progress Report*.

## ***Lack of Effective and Affordable Treatments***

Patients with rare and common cancers alike often lack effective treatment options. Rare cancers collectively comprise 22% of cancer diagnoses worldwide.<sup>5</sup> Yet because each distinct rare cancer only affects a small proportion of patients – and hence offers a small market of potential customers for treatments – for-profit pharmaceutical companies have little incentive to invest in research and development (R&D) for rare-cancer therapeutics. There are more treatment options for patients with common cancers, but the outlook is still far from ideal. For instance, lung cancer is a common cancer, yet patients with late-stage, metastatic lung cancer face a 5-year survival rate of only 5%.<sup>6</sup> Better treatments are clearly needed.

Even when effective treatments exist, patients frequently struggle to afford them. The median monthly listed cost for anti-cancer drugs is around \$10,000, which is more than two times the median monthly household income of \$4,300.<sup>7</sup> Cost barriers can leave patients with no other choice than to skip taking their drugs or ration their medications.<sup>8</sup>

## ***A Solution: Repurpose Generic Drugs***

Drug repurposing presents a remarkable opportunity to provide cancer patients with effective and affordable treatment options. Drug repurposing investigates if a drug that has been approved to treat one disease is also effective for treating a different disease. Generic versions of a drug become available when the drug's patent expires, which in the United States is around 10 years after Food and Drug Administration (FDA) approval. Repurposing generic drugs as is (i.e., without changing the drugs in any way, such as through reformulation) is the fastest way to develop new and low-cost treatments.

The value of drug repurposing comes largely from the time, effort, and cost involved in creating novel drugs from scratch. It can take up to 15 years and \$2 billion to develop one new FDA-approved drug.<sup>9</sup> This is due to the long R&D process for medical interventions and to the fact that a large fraction of drugs fail for safety or efficacy reasons. When repurposing FDA-approved drugs, the first steps of the R&D process – including preclinical studies for discovery and Phase I/II clinical trials for toxicity – can often be skipped. Repurposed drugs are less likely to fail during clinical trials since they have a history of safe patient use.<sup>10</sup> A definitive Phase III clinical trial testing the efficacy of a repurposed drug for treating cancer could cost less than \$10 million and be completed within five years. Repurposed generic drugs could also cut costs post-R&D. While on-patent drugs cost around \$10,000 per month, off-patent generic drugs can cost only a few

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<sup>5</sup> Pillai, R.K.; Jayasree, K. (2017). [Rare cancers: Challenges & issues](#). *Indian J Med Res*, 145(1):17-27.

<sup>6</sup> American Lung Association. (2020). [Lung Cancer Fact Sheet](#).

<sup>7</sup> Prasad, V.; De Jesús, K; Mailankody, S. (2017). [The high price of anticancer drugs: origins, implications, barriers, solutions](#). *Nature Reviews Clinical Oncology*, 14: 381–390.

<sup>8</sup> Patients for Affordable Drugs (n.d.). [Blog](#).

<sup>9</sup> DiMasi, J.A.; Grabowski, H.G.; Hansen, R.W. (2016). [Innovation in the pharmaceutical industry: New estimates of R&D costs](#). *Journal of Health Economics*, 47: 20-33.

<sup>10</sup> Ashburn, T.T.; Thor, K.B. (2004). [Drug repositioning: identifying and developing new uses for existing drugs](#). *Nature Reviews Drug Discovery*, 3(8): 673–683.

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hundred dollars per month. Increasing the number of generics used in cancer treatment could therefore cut cancer-care costs.

There are approximately 1,100 generic drugs approved for medical treatments unrelated to cancer. Thousands of published preclinical and early clinical studies collectively suggest that more than 250 of these existing generics hold promise for treating cancer.<sup>11</sup> We cannot afford to let these potentially life-saving interventions go underutilized.

## ***Lessons from COVID-19***

The public-health crisis caused by the coronavirus pandemic exposed the need and opportunity for drug repurposing. In the race to find COVID-19 treatments, many academic institutions and pharmaceutical companies have investigated repurposed drugs. More than 115 repurposed generic drugs have been or are currently being tested in clinical trials to assess efficacy for treating COVID-19.<sup>12</sup> The generic corticosteroid dexamethasone emerged as the first drug proven to help treat COVID-19, specifically for patients requiring respiratory therapy. Dexamethasone costs only \$1 per day of treatment. Like many generic drugs, dexamethasone is on the World Health Organization (WHO) Model List of Essential Medicines and is available around the world. Using dexamethasone to treat COVID-19 is an example of the rapid impact that generic drug repurposing can have for patients everywhere.

## ***Obstacles to Drug Repurposing***

The biggest obstacle to repurposing generic drugs is the lack of funding for Phase III clinical trials. Phase III trials are designed to provide definitive evidence of the efficacy and safety of interventions. Phase III trials are the most expensive clinical trials to run due to their large size and comparatively long duration. As such, almost all Phase III trials for novel drugs are funded by pharmaceutical companies that have the requisite large amounts of capital on hand and that stand to financially benefit from selling the drugs once approved. However, pharmaceutical companies are not interested in funding trials with generics because selling the existing low-cost drugs for additional uses would not generate enough profit. While novel drugs can be patent-protected (and hence made profitable), patents on new uses of generic drugs are generally not effective.

The federal government has not addressed this market failure. The majority of clinical trials funded by the National Institutes of Health (NIH) are Phase I and II trials. Even the relatively small number of NIH-funded Phase III trials has been decreasing, dropping from 230 Phase III trials in 2005 to just 62 in 2015.<sup>13</sup> Very few of these trials have been funded by the National Cancer Institute (NCI) and focused on cancer. Moreover, the National Center for Advancing Translational Sciences (NCATS) – the division of the NIH that supports drug repurposing – is prohibited from

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<sup>11</sup> Anticancer Fund. (2021). [ReDO\\_DB – Drug Repurposing Database](#).

<sup>12</sup> Reboot Rx. (2021). [COVID-Cancer Project Dataset 2: COVID-19 Drugs and Cancer](#).

<sup>13</sup> Gresham, G.K.; et al. (2017). [Characteristics and trends of clinical trials funded by the National Institutes of Health between 2005 and 2015](#). *Clinical Trials*, 15(1): 65–74.

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funding Phase III trials except for trials focused on rare diseases. Funding for these trials is extremely limited, as NCATS is among the least funded of all the NIH institutes.

A new federal program is needed to fund Phase III cancer trials with repurposed generic drugs. Such a program would be a natural extension of the Cancer Moonshot,<sup>14</sup> making more therapies available to more patients and cutting cancer-care costs across the United States.

## Plan of Action

To improve outcomes for cancer patients and cut cancer-care costs, the Biden-Harris Administration should launch the Repurposing Generics Grant Program through the NCI. The Repurposing Generics Grant Program would fund Phase III clinical trials testing repurposed generic drugs for efficacy in treating cancer. President Biden could include the Repurposing Generics Grant Program in his FY2022 budget proposal, working with Congress to authorize the program and related appropriations at a funding level of \$100 million over 5 years.

### *Program Details*

The Repurposing Generics Grant Program would likely fit best within the NCI but could also be housed at federal entities such as NCATS, the FDA, or even the potential new Advanced Research Projects Agency for Health (ARPA-H).<sup>15</sup> Our proposal for the Repurposing Generics Grant Program is modeled off of the FDA's Orphan Products Clinical Trials Grants Program,<sup>16</sup> which funds the development of products for rare diseases. In short, we propose that the Repurposing Generics Grant Program be established and operate as follows:

- (1) **Hire staff.** The federal agency housing the Repurposing Generics Grant Program would hire grants management and program staff to administer the program. The staff team would manage the application and review process and oversee funded proposals.
- (2) **Determine funding priorities.** The staff team would assemble an external panel of oncologists, researchers, and patient advocates to help determine the types of trials to fund. The panel would develop criteria for prioritizing clinical trials that evaluate treatments for cancer-patient populations with the greatest unmet needs, such as those with poor prognoses and those who have no other accessible treatment options. The program would be set up with consideration for experimental grant-making processes with the intent of maximizing impact through cutting-edge data and artificial intelligence (AI) capabilities.

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<sup>14</sup> "Cancer Moonshot," National Cancer Institute, <https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative>.

<sup>15</sup> "HARPA: Health Advanced Research Projects Agency," HARPA, <https://www.harpa.org/>.

<sup>16</sup> "Orphan Products Clinical Trials Program," U.S. Food and Drug Administration, <https://www.fda.gov/industry/developing-products-rare-diseases-conditions/orphan-products-clinical-trials-grants-program>.

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- (3) **Release a request for proposals.** Members of the scientific community – including academic clinical researchers and pharmaceutical companies – would be invited to submit grant proposals for Phase III clinical trials testing repurposed generic drugs for efficacy in treating cancer. The proposals would need to specify the scientific rationale for the drug to be used for the target cancer-patient population, outline a clinical trial protocol, and present a budget.
- (4) **Evaluate applications.** The external panel would evaluate proposals for scientific and technical merit. The feasibility of widespread clinical adoption for proposed treatments would also be considered. Scores would be assigned to each application for comparison purposes and a minimum of five proposals would receive funding during the 5-year program. Each funded proposal would receive a grant of between \$10 and \$20 million to cover Phase III trial costs.
- (5) **Ensure reporting.** A program officer would oversee activities of each grantee during the funding period. Grantees would be required to periodically submit reports on the progress of their funded trials. Following completion of the trials, grantees would submit final reports describing the results and plans for driving awareness of the data. The agency housing the Repurposing Generics Grant Program would provide an annual report to Congress on the program’s status.

## *Impact*

The Repurposing Generics Grant Program would generate the evidence needed to use repurposed generic drugs as part of the standard of care for cancer. The result would be effective new cancer therapies that are accessible to everyone. In addition, the program would provide proof that repurposing generic drugs is a viable strategy to get new treatments to patients faster, accelerating medical breakthroughs across the board. Finally, by providing funding for Phase III clinical trials with generic drugs, the Repurposing Generics Grant Program would create a “push” incentive for researchers and companies to pursue new treatments that otherwise would not be developed due to a market failure.

## Conclusion

President Biden has long been a champion of progress in cancer diagnosis, treatment, and prevention, and of making sure the best possible healthcare is accessible to all. The Repurposing Generics Grant Program would help achieve these goals. The Biden-Harris Administration should prioritize the creation of the Repurposing Generics Grant Program for the benefit of cancer patients who don’t have time to wait.

## Frequently Asked Questions

### **Why should the Repurposing Generics Grant Program focus on cancer and not other diseases?**

Cancer foundations and governments have funded thousands of preclinical and early clinical studies where non-cancer generic drugs were tested for efficacy against cancer. The nonprofit Reboot Rx is building AI technology to find relevant studies on the repurposing of generic drugs, extract key information, and rank drug-cancer pairs based on the evidence. This effort has identified around 500 completed Phase II randomized controlled trials that have collectively tested 100 non-cancer generic drugs for efficacy against cancer. Some of these drugs could go straight into definitive Phase III trials.

In short, the number of known drug repurposing opportunities for cancer far exceeds the number of known repurposing opportunities for other diseases. As more data becomes available to support drug repurposing for other diseases, the Repurposing Generics Grant Program could serve as a model for future programs to support clinical testing of those treatments as well.

### **How would generics that are proven to be effective in Phase III trials be added to the standard of care for cancer?**

The Repurposing Generics Grant Program would focus on generic drugs that are already FDA-approved, on the market, and widely available for other diseases. The program would gather the evidence needed for these existing generics to also be used for cancer treatment. Incorporating a generic that is proven to be effective into the standard of care may include FDA approval and updating the drug labels for the new cancer indication, depending on the will of generic drug manufacturers. We note, though, that off-label use of FDA-approved drugs is legal. Indeed, off-label uses account for many treatments that are considered part of the standard of care for cancer, listed in national treatment guidelines, and covered by insurance. The FDA recently launched Project Renewal<sup>17</sup> to update the labels of old drugs that are part of the standard of care for cancer but do not have the cancer indication on their labels.

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<sup>17</sup> "Project Renewal," U.S. Food & Drug Administration, <https://www.fda.gov/about-fda/oncology-center-excellence/project-renewal>.

## About the Authors



**Laura Kleiman** is the Founder and CEO of Reboot Rx, the tech nonprofit startup dedicated to saving the lives of cancer patients with repurposed generic drugs. Reboot Rx is building AI technology to rapidly review the extraordinary amount of data on generics and identify the most promising drugs for repurposing. By bringing together stakeholders, Reboot Rx is developing new models for funding clinical trials and for incorporating generics into the standard of care for cancer patients.

Laura's career has focused on building collaborations across disciplines and sectors to expand treatment options for cancer patients. She was previously Scientific Research Director in the Department of Data Sciences at the Dana-Farber Cancer Institute. Laura earned a Ph.D. in Computational and Systems Biology from MIT and conducted translational cancer research as an American Cancer Society Postdoctoral Fellow at the Massachusetts General Hospital and Harvard Medical School. She was recently featured in Forbes and received the 40 Under 40 in Cancer Award.



**Shruthi Bhimaraju** is a student at the University of Virginia studying the health sciences and public health. To improve the quality of care for diverse patient populations, she explores the intersection between health policy and social entrepreneurship. As such, she aids the American Cancer Society Cancer Action Network in their mission to lobby for impactful policies and provides cancer education resources to communities across the country. As a Health Policy Researcher at Reboot Rx, Shruthi studies new funding models to help fast-track the development of more affordable cancer treatments. While her clinical experiences fuel her aspirations for a medical career, her ultimate goal is to use her voice to reform the healthcare system to be more equitable.



## About the Day One Project

The Day One Project is dedicated to democratizing the policymaking process by working with new and expert voices across the science and technology community, helping to develop actionable policies that can improve the lives of all Americans. For more about the Day One Project, visit [dayoneproject.org](https://dayoneproject.org)