

# America's Biopharmaceutical Research Companies Are Committed to Fighting Mental Illness

## But The Inflation Reduction Act Could Disrupt The Pipeline Of New Medicines

The United States is facing a growing mental health crisis. Patients desperately need and deserve access to new, innovative therapies to address the growing burden of mental illness.

### BY THE NUMBERS:

#### More than one in 20

Americans have a serious mental illness, which reduces average life expectancy by 10 years.<sup>i</sup>

Major Depressive Disorder is the **second leading cause of disability in the United States**.<sup>ii</sup>

#### 7 million

Americans have bipolar disorder.<sup>iii</sup>

#### 1.5 million

Americans have schizophrenia.<sup>iv</sup>

#### Nearly one-third

of patients with major depressive disorder and nearly one-third of those with schizophrenia are defined as having treatment-resistant forms of these illnesses.<sup>ii, v</sup>

Unfortunately, researching and developing medicines to treat mental illness have some of the lowest probabilities of success. This is in large part due to a limited understanding of brain mechanisms that drive these illnesses, the neurochemical pathways involved and the role they play in these illnesses. This limited scientific understanding, combined with the extremely diverse nature of the diseases themselves—which often manifest differently in different people—have made it difficult to identify biomarkers that can aid in diagnosis, research, development and treatment of medicines for mental illnesses.<sup>vi</sup> In addition, there are significant recruitment and retention challenges associated with conducting clinical trials in patients who struggle with these illnesses.

### As a result of these challenges:

- It takes **20% longer** to develop a drug treating the central nervous system (CNS) and **38% longer** for these medicines to receive regulatory approval.<sup>vii</sup>
- Clinical trial success rates for medicines treating the CNS are **just 6.2%**, well below the average for other conditions not impacting the CNS (13.3%).<sup>viii, ix</sup>

Despite the incredible challenges, there are currently **163 medicines in development** that are seeking to treat those living with mental illness.<sup>x</sup> Unfortunately, it is unclear whether these advances will continue to be pursued given additional risks and uncertainty posed by price setting provisions in the Inflation Reduction Act which threatens progress against mental illness.

The price setting provisions in the IRA discourage the research and development needed to bring forward new medicines to address the growing burden of mental illness.

### For example, the IRA:

- **Discourages development of small molecule medicines and those covered under Medicare.**
  - o The IRA discourages research and development investments in mental illness due to the high rates of serious mental illness in elderly and disabled Americans who receive drug coverage under Medicare, where medicines will be selected for government price setting.

o Small molecule medicines are the primary source of treatment options for mental illness due to their unique ability to cross the blood-brain barrier. Provisions in the IRA specifically undermine the development of small molecule medicines by allowing them to be price set just 9 years after initial U.S. Food and Drug Administration (FDA) approval, about 4-5 years shorter than the average timeframe medicines currently have on the market before facing generic competition.

•  **Ignores the critical research and development that occurs in the years following FDA approval.**

- o Post-approval research and development results in real innovations that improve patients' lives and is particularly important to the development of medicines for mental illness.
- o Many mental illnesses are highly related. Therefore, it is not uncommon for medicines to continue to be researched and developed for potential use across multiple mental illnesses or patient populations after initial FDA approval.
- o The shorter timeframe imposed by the IRA price setting provision puts this type of resource intensive research and development at risk.

**Biopharmaceutical companies are committed to continued research and development for mental illnesses that are having to make hard choices about their investments because of the IRA. In a recent survey:**<sup>xi</sup>

- **82%** of biopharmaceutical companies with research projects in areas including mental health expect substantial impacts on their pipeline.
- **63%** of companies say they will have to shift R&D investment away from small molecule medicines.
- **95%** expect to develop fewer new uses of already approved medicines.

With the IRA, the government is telling companies they can no longer follow promising science and discouraging the development of medicines that could help address our country's mental health crisis.

## Case Study

The following case study illustrates a previously approved medicine that may have not come to market for patients with mental illnesses if the IRA's price setting provisions had been in place when the biopharmaceutical company who developed this medicine was considering the feasibility of bringing it to market. This is particularly true given the relatively limited timeframe now afforded under the IRA to be able to conduct clinical trials for more than one mental illness or treatment population and to be able to recoup the costs of that research.

**Antipsychotic Provides Critical Treatment for Schizophrenia and Bipolar Depression in Both Adults and Children.** Latuda (lurasidone) is an atypical antipsychotic treatment originally FDA-approved to treat adults with schizophrenia in 2010. One year prior to this approval, clinical trials were initiated to research Latuda for use in adults with depressive episodes associated with bipolar depression and in 2013, this use was also FDA-approved.<sup>xii</sup> Subsequently, additional clinical trials led to the approval of Latuda in adolescents with schizophrenia (13-17 years old) in 2017 and in pediatric patients (10-17 years old) with bipolar depression in 2018.<sup>xiii</sup>

The Latuda clinical development program involved several years of research, significant risk, and substantial financial investment in order to obtain FDA approval for the initial use as well as each subsequently approved use. Unfortunately, this type of clinical development program may be deemed cost prohibitive in a post-IRA world given the limited timeframe by which to recoup the costs of these investments, the R&D challenges and the low probabilities of success in this therapeutic area.

i Hayford, D. P. et al (2019, February 1). Medicare Advantage and commercial prices for Mental Health Services: Health Affairs Journal. Health Affairs. Retrieved October 7, 2022, from <https://www.healthaffairs.org>

ii Zhdanova M, Pilon D, Ghelertler J, et al. The prevalence and national burden of treatment-resistant depression and major depressive disorder in the United States. J Clin Psychiatry. 2021;82(2):20m13699. <https://doi.org/10.4088/JCP.20m13699>

iii <https://journal.bipolar-disorders.springeropen.com/articles/10.1186/s40345-021-00225-5>

iv <https://www.nami.org/About-Mental-Illness/Mental-Health-Conditions/Schizophrenia>

v de Bartolomeis A, Ciccarelli M, Vellucci L, Fornaro M, Iasevoli F, Barone A. Update on novel antipsychotics and pharmacological strategies for treatment-resistant schizophrenia. Expert Opin Pharmacother. 2022 Dec;23(18):2035-2052.

vi Hyman SE. Revitalizing psychiatric therapeutics. Neuropsychopharmacology. Jan 2014;39(1):220-9. doi:10.1038/npp.2013.181

vii Tufts Center for the Study of Drug Development. See [press release](#) summarizing study results. 2018.

viii Gribkoff VK, Kaczmarek LK. The Need for New Approaches in CNS Drug Discovery: Why Drugs Have Failed, and What Can Be Done to Improve Outcomes. Neuropharmacology. 2017;120:11-19. doi:10.1016/j.neuropharm.2016.03.021.

ix Geils H, Lavelle T, Riley A. Incentivizing Drug Development for Serious Mental Illness, Tufts, Center for the Evaluation of Value and Risk in Health. January 2022. <https://cevr.tuftsmedicalcenter.org/news/20227smi>

x More than 160 medicines in development for mental illness. PhRMA. 26 Jan 2023. <https://catalyst.phrma.org/new-report-more-than-160-medicines-in-development-for-mental-illness>

xi Inflation Reduction Act Already Impacting R&D. PhRMA. 13 Jan 2023. <https://www.phrma.org/resource-center/Topics/Economic-Impact/Inflation-Reduction-Act-Already-Impacting-R-and-D>

xii Azhar Y, Shaban K, Lurasidone. [Updated 2022 Jun 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK541057/>

xiii [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/200603s035lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/200603s035lbl.pdf)