IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civil Action No. 23-931-CFC

DECLARATION OF JIM ADER

1. I, Jim Ader, submit this Declaration on behalf of AstraZeneca Pharmaceuticals LP and AstraZeneca AB (collectively, AstraZeneca) in opposition to Defendants' Cross-Motion for Summary Judgment.

2. I am over the age of 18. Except as expressly indicated, the facts stated herein are based upon my personal knowledge, including my work at AstraZeneca,

and my general experience in the pharmaceutical industry. If called to testify, I could truthfully and competently testify to those facts.

3. I am the Vice President of U.S. Market Access at AstraZeneca, where I have been employed for 24 years. I have more than 31 years of experience in the pharmaceutical industry. During that time, I have held a variety of roles in market access and sales at several different pharmaceutical companies.

4. In my current position, I lead the U.S. Market Access team across AstraZeneca's BioPharmaceutical Business Unit. I also serve as a member of the US Leadership Team.

5. As a result, I am familiar with the concrete and imminent harm that will befall AstraZeneca as a direct result of CMS's implementation of the Drug Price Negotiation Program (DPNP) provisions of the Inflation Reduction Act (IRA).

6. AstraZeneca is a global, science-led, patient-focused pharmaceutical company. We are dedicated to transforming the future of healthcare by unlocking the power of what science can do for people, society and the planet.

7. AstraZeneca therefore invests significant time and money to identify, test, and develop new drug candidates with the goal of helping patients live longer and better lives. It can take decades and hundreds of millions of dollars to shepherd a single potential new therapy through clinical trials. Even when a drug

shows early promise, FDA's rigorous drug approval process means very few of those early drug candidates are ever approved and commercialized. Studies estimate that only one of every 5,000 compounds that enters preclinical testing will achieve FDA approval—a failure rate of 99.98%.

8. On August 29, 2023, the Centers for Medicare & Medicaid Services (CMS) selected AstraZeneca's drug product FARXIGA® (dapagliflozin) for negotiation under the Drug Price Negotiation Program.

9. On or before October 1, 2023, as required by the statute, AstraZeneca signed a Manufacturer Agreement drafted by CMS that spells out how the negotiation process will play out. Exhibit 1. The Agreement gave the agency unilateral authority to make changes to its terms to reflect changes in "law, regulation, or guidance." *Id.* at IV.B. Any breaches of the Agreement or failures to meet the requirements of the Drug Price Negotiation Program will result in "civil monetary penalties and an excise tax, as applicable." *Id.* at IV.J.

10. On or before February 1, 2024, CMS will send out an initial offer of a Maximum Fair Price, and AstraZeneca will be forced to respond before **March 2, 2024**.

11. AstraZeneca therefore is forced to make a number of decisions now about its willingness to go forward with its participation in the program—and it has no choice but to do so based on the policies that CMS has announced will apply in

the first initial price applicability year (IPAY), 2026. If AstraZeneca were to withdraw from both Medicare and Medicaid participation—not just for FARXIGA, but for all of its drug products—it would have an enormous financial consequence for the company. Medicare and Medicaid collectively cover 30% of the American population and 50% of all U.S. prescription drug sales.

12. The penalty is particularly high for those AstraZeneca drug products that cater to patient populations disproportionately covered by Medicare Part B. For example, AstraZeneca's IMFINZI® (durvalumab), an immunotherapy designed to treat certain cancers, is heavily Medicare-dependent. The vast majority of its patient population—over 50%—is comprised of Medicare beneficiaries.

13. Medicare and Medicaid collectively account for approximately more than 40% of AstraZeneca's gross revenues in the U.S. .

14. AstraZeneca, no less than any other drug manufacturer, can ill afford to withdraw from federal programs that make up approximately half of all spending in the prescription-drug market.

HARMS DUE TO QUALIFYING SINGLE SOURCE DRUG DEFINITION

15. CMS's Qualifying Single Source Drug definition harms AstraZeneca in several ways. First, the agency's policy ensures that if any future therapies share the same active moiety as a selected drug product, those products will immediately be subject to the Maximum Fair Price the agency has already established for the selected product.

16. It is a core value of AstraZeneca to follow the science and continuously explore new potential uses of the active moieties of its already-approved drug products. To be clear, AstraZeneca must still devote a lot of work, effort, time, and resources to obtaining approval for a new indication for or formulation of an already-approved active moiety, often including clinical trials. By subjecting two or more AstraZeneca products approved under separate New Drug Applications (NDAs) or Biologics License Applications (BLAs) to the same Maximum Fair Price, CMS's Qualifying Single Source Drug definition diminishes incentives for AstraZeneca to invest in future therapies and treatments for the active moiety of a selected drug product.

17. FARXIGA provides a good example. FDA first approved FARXIGA in 2014 as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes. AstraZeneca's continued investment in FARXIGA has resulted in subsequent FDA approvals over the years to treat a variety of diseases.

Each of these supplemental approvals has saved and improved patients' lives by making available new treatments that FDA has found to be safe and effective.

18. In October 2019, FDA approved FARXIGA as a treatment to reduce the risk of hospitalization for heart failure in adults with Type 2 diabetes and established cardiovascular disease or multiple cardiovascular risk factors. The approval was a significant development for Type 2 diabetes patients; heart failure is often one of the first cardiovascular complications a Type 2 diabetes patient will experience, and FDA's supplemental approval allowed physicians to act sooner by prescribing FARXIGA, thereby reducing patients' risk of hospitalization for heart failure.

19. In May 2020, FDA further approved FARXIGA as a treatment to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (New York Heart Association class II-IV) with reduced ejection fraction. This approval gave physicians a new treatment option to greatly improve outcomes in heart-failure patients with reduced ejection fraction.

20. FDA again issued new approvals in April 2021, approving FARXIGA as a treatment to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression. This milestone approval marked the most significant advancement in

the treatment of chronic kidney disease in more than two decades. It gave patients and physicians a new and effective treatment option to combat an often debilitating and life-threatening disease.

21. Just this past spring, in May 2023, FARXIGA was approved as a treatment to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure. This most recent FDA approval made it possible for patients across the full spectrum of heart failure, regardless of left ventricular ejection fraction status, to benefit from FARXIGA.

22. So far, all of these additional approvals were associated with the original NDA for FARXIGA. However, if there are enough differences between the original formulation and/or indication and the new formulation and/or indication, or in the drug products themselves, FDA will require a new therapy to be approved under a new NDA.

23. While clinical trials are currently focused on "combination product" therapies that would not be impacted by the agency's definition of Qualifying Single Source Drug, there are other ongoing drug development efforts involving the same active moiety as FARXIGA where one development pathway could result in the product being treated as the same QSSD as FARXIGA under CMS's position.

24. Another example is AstraZeneca's drug LYNPARZA® (olaparib), a small-molecule cancer medicine that was first FDA-approved in capsule form in 2014. Over time, AstraZeneca continued to invest in the drug, developing a formulation that was better tolerated by patients, resulting in FDA approval for a tablet form under a different NDA in 2017. The tablet form expanded the patient population able to benefit from the active ingredient, because it could be taken with certain other medicines.

25. Similarly, AstraZeneca's drug CALQUENCE® (acalabrutinib), a leukemia medicine, was approved in capsule form in 2017. FDA separately approved a tablet form of CALQUENCE under a different NDA in 2022. The tablet formulation expanded the patient population able to benefit from CALQUENCE because, unlike the capsule, it may be taken with gastric acid-reducing agents.

26. CMS's definition of Qualifying Single Source Drugs dramatically alters manufacturers' incentives to invest in such follow-on therapies using a previously approved active moiety. Under the agency's approach, a product approved under a different NDA with the same active moiety as a selected drug product will now be treated as the same drug, and immediately become subject to the Maximum Fair Price. Under the agency's definition, AstraZeneca would have

no incentive to spend years and a steep financial investment researching alternative treatment uses for the active moiety of a selected product.

HARMS DUE TO BONA FIDE MARKETING STANDARD

27. FARXIGA will experience generic competition sometime between October 2025 and Summer 2026. FDA has already granted tentative approval to 17 generic versions of FARXIGA. A tentative approval means that FDA has determined that the product meets the requirements for approval but must await expiration of either patent rights or market exclusivity periods before it may lawfully enter the market. Once all patents and exclusivities for FARXIGA expire, FDA will convert the tentative approvals to final approvals and there will be no legal impediment to the generic products entering the market.

28. If AstraZeneca is forced to sell FARXIGA at the agency's compelled below-market price while *also* facing generic competition, the financial losses suffered by AstraZeneca will be significant. That harms AstraZeneca—and in turn will adversely affect AstraZeneca's ability to invest in follow-on therapies as well as other drug products, to the detriment of patients.

HARMS DUE TO IMPACT ON DRUG DEVELOPMENT EFFORTS

29. These harms are not limited to the impact on FARXIGA. Over the next three years, CMS will select up to 50 additional drugs to be eligible for the

Drug Price Negotiation Program. That selection process will very likely sweep up more of AstraZeneca's drug products.

30. For example, AstraZeneca's CALQUENCE is a potential candidate for selection in 2025 for IPAY 2027. Thus, even pre-selection, AstraZeneca has to make investment decisions now on research development of follow-on therapies for new indications and improvements to the drug itself.

31. Because it is unclear whether CMS will ever change its policies on the issues challenged in this lawsuit, AstraZeneca must assume those policies will continue absent judicial intervention.

32. AstraZeneca has thus been forced to make decisions now based on the agency policies currently in place. In this way, the policies will impact the company's drug development and commercialization for years to come.

I declare under penalty of perjury pursuant to 28 U.S.C. § 1746 that the foregoing is true and correct.

DocuSigned by:
James Ader
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December 1, 2023