INTRODUCTION

Background
After initial approval by the U.S. Food and Drug Administration (FDA), approximately one-third of drugs undergo clinical trials in new patient populations towards additional indications. Research into new indications provides patients with expanded treatment options and promotes accessibility by facilitating payer reimbursement. The Inflation Reduction Act of 2022 (IRA) introduces price setting for drugs with the highest gross total spending in the Medicare program at 9 and 13 years post-initial FDA approval for small molecules and biologics, respectively. To describe the landscape of post-FDA approval clinical development for high-spend Medicare Part D small molecule drugs and illustrate the potential impact of the IRA on research and development (R&D) investments towards subsequent indications.

Objective
To conduct a retrospective study of post-FDA approval clinical trials for small molecule drugs, and to evaluate the landscape of post-FDA approval clinical trials and the subsequent indications that these drugs receive. The study includes an analysis of the impact of the IRA on post-FDA approval clinical trials and subsequent indications.

Methods
The study included all small molecule drugs that were approved in the United States between 2020 and 2019, and had at least one additional indication in the previous 10 years. Clinical trials for each drug were identified, and the number of trials completed before and after the additional indication was noted. The time from initial FDA approval to the first post-FDA approval clinical trial, and the time from the first post-FDA approval clinical trial to the next post-FDA approval clinical trial, was also recorded. The number of post-FDA approval clinical trials and the number of subsequent indications for each drug were counted, and the relationship between these metrics and the IRA was assessed.

Results

- 20 Unique New Small Molecule Drugs
- 41 Subsequent Indications based on Post-Approval Clinical Trials

- 75% Oncology
- 25% Initial Indication: Orphan Designation
- 32% Orphan Designation or Extension of Initial Orphan Designation

Conclusions & Policy Implications
A significant amount of drug development occurs after initial FDA approval. Among drugs studied, post-approval clinical trials started on average 3.1 years after initial approval, with subsequent indications receiving FDA approval on average 7.5 years after a drug was first approved by the FDA. Nearly a quarter (n = 10, 24.4%) of the subsequent indications received FDA approval more than nine years after the initial approval. The case study above features investments in clinical trials towards subsequent indications. The Inflation Reduction Act of 2022 (IRA) introduces price setting for drugs with the highest gross total spending in the Medicare program at 9 and 13 years post-initial FDA approval for small molecules and biologics, respectively. These policies may have unintended consequences on patient access to medicines.

- Clinical trials towards a new indication were registered, on average, 3.1 years after initial approval.
- Subsequent indications based on post-approval clinical trials received FDA approval, on average, 7.5 years after a drug was first approved by the FDA.
- Nearby a quarter (n = 10, 24.4%) of the subsequent indications received FDA approval more than nine years after the initial approval.

References
- James Motyka, PharmD; Julie Patterson, PharmD, PhD; Sharon Phares, PhD, MPH; National Pharmaceutical Council, Washington, DC, USA.