

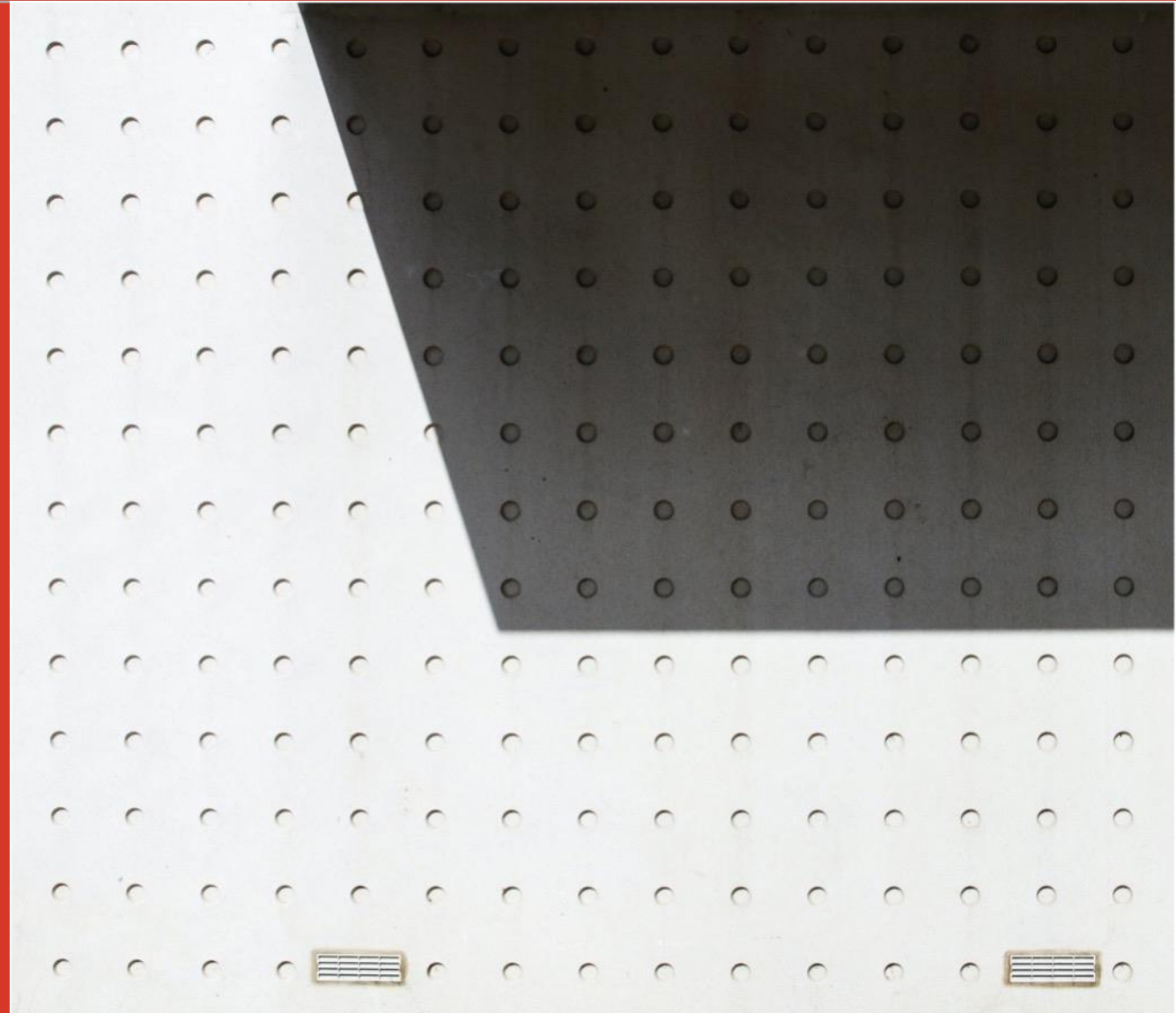
# The First 10 Drugs to be Negotiated by Medicare

On August 29, the Centers for Medicare & Medicaid Services announced the first 10 drugs to be negotiated by Medicare. As CMS and pharmaceutical manufacturers prepare for negotiations, they will consider not only the effectiveness of these drugs, but also their financial performance and investment over the years.

To create a public benchmark of these measures, ATI collected data from [FDA](#) labels, [Evaluate](#) Pharma and Omnium databases, the CMS spending [dashboard](#), and proprietary data. For each drug, we present a high-level summary of its time on the market, use in Medicare, clinical development activity and investment, global and US sales, its position in the manufacturer's portfolio, and deal history.

*This work is supported by Arnold Ventures.*

**ATI Advisory**



## Our Findings

- On average, selected drugs have been on the market for 13.8 years. Two drugs, Enbrel and Novolog, have been on the market for more than 20 years.
- Only one drug, Imbruvica, is in a protected class. This guarantees its placement on Part D formularies and shields it from competition with other drugs. Most of the remaining drugs, which are indicated for more common conditions, such as autoimmune conditions, heart failure and cardiovascular disease, and diabetes, do face head-to-head competition.
- Competition means rebates, which translates to a lower ceiling in negotiation than the statutory discounts in the IRA, leading to lower negotiated prices.

### Sales

- To date, cumulative global sales for these drugs are \$481 billion, of which \$265 billion, or 55% are attributable to the US.
- Several of these drugs are major drivers of their company's earnings. Eliquis, Enbrel, Jardiance, and Stelara accounted for at least 20% of their company's U.S. pharmaceutical sales.

### Clinical development

- We did not estimate R&D spending for Novolog and Enbrel because their development preceded modern clinical trial reporting standards.

- Total estimated R&D spending across the remaining drugs is \$34.3 billion, or 11% of their global sales revenues. Spending estimates ranged from \$1.4 billion for Imbruvica to \$7.8 billion for Xarelto.
- Phase I-IV trials for these drugs included over 630,000 subjects.
- Clinical trial activity and spending was unevenly distributed over time. On average, 61% of R&D costs were incurred after a drug's approval. Eliquis (32%), Entresto (47%), and Jardiance (47%) were the only drugs for which post-approval spending fell below pre-approval amounts. By contrast, direct competitors Xarelto (for Eliquis) and Farxiga (for Jardiance) spent 58% and 67%, respectively, during the post-approval period.

### Generic/biosimilar competition

- Several drugs, including Stelara and Januvia, are expected to have generic or biosimilar competitors by the time the negotiated prices go into effect. These drugs will be negotiated, but if a generic or biosimilar demonstrates adequate uptake in Part D, they may not become subject to the negotiated price.

For more information, please contact Robert Shalett, Director of Communications, [Robert@atiadvisory.com](mailto:Robert@atiadvisory.com).

[Eliquis](#) →

[Enbrel](#) →

[Entresto](#) →

[Farxiga](#) →

[Imbruvica](#) →

[Januvia](#) →

[Jardiance](#) →

[Novolog](#) →

[Stelara](#) →

[Xarelto](#) →

[Appendix](#) →

## Discussion: Spending on Clinical Development

R&D spending estimates in our report appear to be orders of magnitude greater than commonly cited benchmarks, which range from \$1.3 - \$2.5 billion. However, there are important differences in our approach. Previous studies estimate the cost of developing a new drug up to FDA approval. We estimate all spending attributable to Phase I-IV clinical studies of drugs selected for negotiation, including costs incurred post-approval. Considering only pre-approval estimates (\$320 million - \$3 billion), our findings are well within the range of previous studies.

Post-approval studies contribute dramatically to overall R&D spending in our estimates. On average, 61% of spending on clinical studies was incurred after these drugs received their first FDA approval. These studies differ from those done to gain initial FDA approval. After launch, companies usually conduct Phase III or IV studies, which cost more and enroll more study participants than earlier phases. Their purpose is not to develop a new drug, but to facilitate the marketing of an existing one – satisfying post-marketing requirements from the FDA, adding new indications, or demonstrating a drug's value to payers (not all trials are done for the FDA's benefit).

Our findings are also directionally consistent with trade press suggesting that competition among drugs is driving greater post-launch R&D efforts. For example, Farxiga's recent studies in heart failure differentiate it from other drugs in its class. The makers of Xarelto, which competes with market-leader Eliquis, have invested heavily in clinical studies to expand its label, adding numerous indications over the years.

As manufacturers prepare to submit their data to CMS, they may include spending on these types of studies. CMS, in turn, will have to determine whether they merit consideration. It may not matter, either way, since even at these high R&D spending estimates, companies made significant and sustained returns on investment.

Nevertheless, it's important to bear in mind that R&D to bring a new drug to market is different from R&D to advance its position in that market. It's generally less risky to spend money on

expanding the market for an existing drug, particularly one that promises to be a blockbuster, than one that has yet to stand the test of FDA review. By the time a drug is on the market, revenues accrue, and the manufacturer's R&D team has more experience to guide development towards subsequent indications.

There is undoubtedly value in adding new indications and better understanding how well a drug works, under what circumstances and for which patients. Manufacturers assert that under negotiation, added indications may become less attractive as investments. Arguments in this vein should be weighed carefully against other opportunity costs. For example, the more of a manufacturer's R&D budget is dedicated to the perpetuation of an existing product, the less is spent on developing new ones. The reverse is also true – companies that need to replace revenues from aging blockbusters tend to increase spending on new drug development.

To date, most efforts to evaluate R&D spending have focused on quantifying the investment necessary to bring a drug to market. Far less has been written about the economics of post-launch trials, which will take on increasing importance as manufacturers jockey to demonstrate value and improve their negotiating position with Medicare. Our findings suggest that these studies will take on more prominence as negotiation evolves and raises questions about the relative value of different types of R&D efforts.

Please see [Methods](#) for additional detail on Evaluate clinical trial and R&D spending data used in this report


# Eliquis

(apixaban)

**Bristol-Myers Squibb / Pfizer**

Originator: DuPont Pharmaceuticals

Tablets for oral use | small molecule



### Indications

✓ Factor Xa inhibitor anticoagulant indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

### Clinical Development

**135,171** Participants enrolled in the **48 clinical trials** WW evaluating Eliquis

**54%** of clinical trials started post FDA approval

**\$4.3B** Estimated R&D spend

**Active Programs**

Phase III
<ul style="list-style-type: none"> <li>Arterial thrombosis</li> <li>Atrial fibrillation</li> </ul>

**Investments in Trials by Study Start Date**

	Pre-approval	Post-approval
<b>Trial Cost</b>	\$3.0B	\$1.4B

### Patents and Exclusivity

<b>Expected loss of exclusivity</b>	2028
<b>Years on the market</b>	9.7

### Other Drugs in Therapeutic Class

**Xarelto**  
Bayer/J&J  
\$2.5B in US Sales, 2022

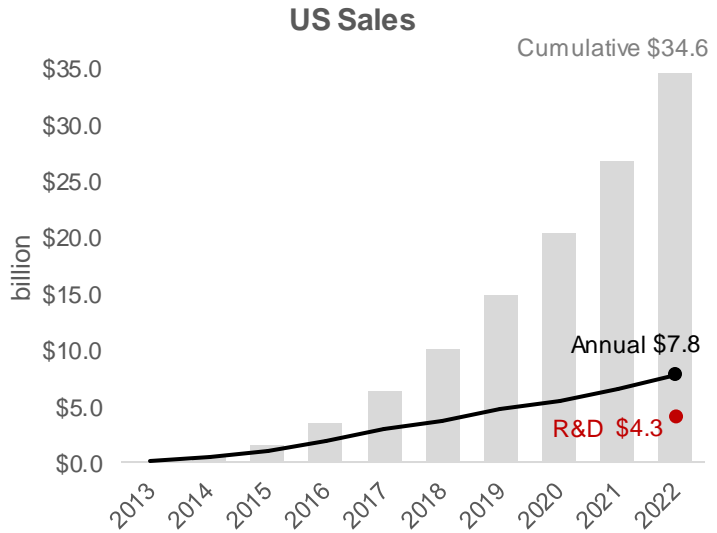
**Lixiana**  
Daiichi Sankyo  
\$23M in US Sales, 2022

### Medicare Part D, 2021

<b>\$12.6B</b>	<b>3,125,087</b>
<b>Total Gross Spending</b>	<b>Total Beneficiaries</b>

### Portfolio Position

<b>25%</b>	<b>#2</b>	<b>\$57.1B</b>
<b>of Bristol-Myers Squibb's US Rx Sales, 2022</b>	<b>Sales Rank, 2022</b>	<b>Global Lifetime Sales</b>



**Key Events**

**2001:** Bristol-Myers Squibb acquires DuPont Pharmaceuticals for **\$7.8 bn**

**2007:** Bristol-Myers Squibb and Pfizer agree to a development and commercialization deal

**2011:** First launch in EU (9/19)


**2012:** FDA approval and US launch for stroke prophylaxis secondary to atrial fibrillation (12/28)

**2014:** Added indications for pulmonary embolism and deep vein thrombosis

# Enbrel

(etanercept)

**Amgen**



Originator: Immunex  
Injections | Biologic

**Indications**

- ✓ Rheumatoid arthritis (RA)
- ✓ Polyarticular juvenile idiopathic arthritis (JIA) in patients aged 2 years or older
- ✓ Psoriatic arthritis (PsA)
- ✓ Ankylosing spondylitis (AS)
- ✓ Plaque psoriasis (PsO)

**Clinical Development**

Historical data on clinical development is limited because FDA approval for this drug preceded clinical trial reporting requirements.

**Patents and Exclusivity**

Expected loss of exclusivity	2029
Years on the market	24.8

**Other Drugs in Therapeutic Class**

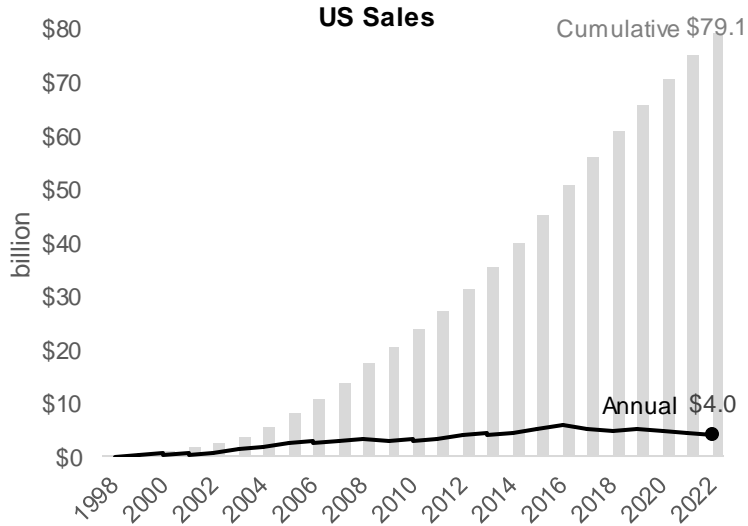
<b>Humira</b> AbbVie \$18.6B in US Sales, 2022	<b>Cimzia</b> UCB \$1.5B in US Sales, 2022	<b>Remicade</b> J&J \$1.5B in US Sales, 2022
<b>Simponi</b> J&J \$1.2B in US Sales, 2022		

**Medicare Part D, 2021**

<b>\$2.4B</b> Total Gross Spending Sureclick, Mini, Enbrel packages	<b>47,739</b> Total Beneficiaries
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**Portfolio Position**

<b>23%</b> of Amgen's US Rx Sales, 2022	<b>#1</b> Sales Rank, 2022	<b>\$132.5B</b> Global Lifetime Sales
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**Key Events**

- 1998:** Enbrel receives FDA approval and launches in US (11/2) for RA; Immunex (originator) and Wyeth-Ayerst enter into a co-promotion agreement in US & Canada.
- 1999:** FDA approves new indication for JIA
- 2002:** Amgen acquires Immunex for \$10bn; FDA approves use in PsA
- 2003:** FDA approves new indication for AS
- 2004:** FDA approves new indication for PsO
- 2009:** Pfizer acquires Wyeth (AHP); Amgen and Pfizer continue co-promotion agreement
- 2012:** Amgen and Pfizer dissolve partnership as Pfizer launches competitor (tofacitinib, Xeljanz)


# Entresto

(sacubitril / valsartan)

**Novartis**

Originator: Ciba-Geigy

Tablets for oral use | small molecule



### Patents and Exclusivity

Expected loss of exclusivity	2025
Years on the market	8.1

### Medicare Part D, 2021

<b>\$1.7B</b>	<b>394,848</b>
Total Gross Spending	Total Beneficiaries

### Indications

✓ Indicated to reduce risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure. Benefits are most clearly evident in patients with left ventricular ejection fraction below normal.

### Other Drugs in Therapeutic Class

### Portfolio Position

<b>15%</b>	<b>#2</b>	<b>\$14.3B</b>
of Novartis' US Rx Sales, 2022	Sales Rank, 2022	Global Lifetime Sales

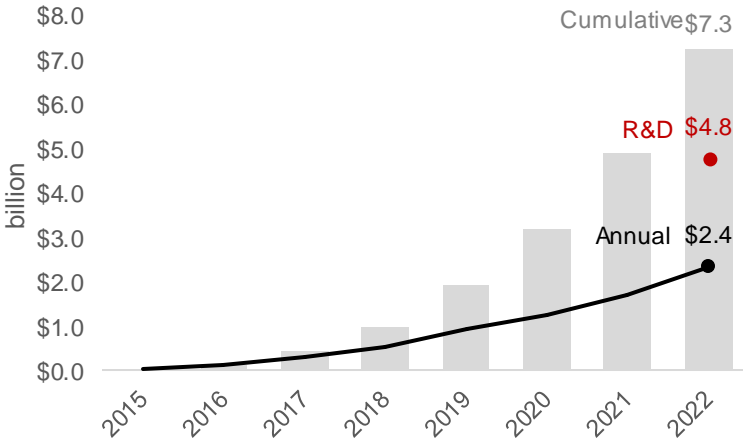
### Clinical Development

**36,572** Participants enrolled in the **51 clinical trials** WW evaluating Entresto

**47%** of clinical trials started post FDA approval

**\$4.8B** Estimated R&D spend

### US Sales



#### Active Programs

Phase III
<ul style="list-style-type: none"> <li>Hypertrophic cardiomyopathy</li> <li>COVID-19 treatment</li> </ul>

#### Investments in Trials by Study Start Date

Trial Cost	Pre-approval	Post-approval
	\$2.5B	\$2.3B


**Key Events**

- 1996:** Ciba-Geigy and Sandoz merge to form Novartis
- 2015:** FDA approval and US launch for chronic heart failure (7/7)
- 2019:** FDA approves use in children with heart failure, granting pediatric exclusivity (10/1)
- 2021:** FDA approves heart failure w/reduced ejection fraction and preserved ejection fraction (2/21)
- 2023:** District court rules patent on combination of sacubitril/valsartan invalid, Novartis announces decision to appeal

# Farxiga

(dapagliflozin)

**AstraZeneca**



Originator: Bristol-Myers Squibb

Tablets for oral use | small molecule

**Indications**

- ✓ Type 2 diabetes (T2DM): Adjunct to diet and exercise to improve glycemic control
- ✓ Heart Failure: Reduce risk of hospitalization, cardiovascular death
- ✓ Treatment of Chronic Kidney Disease (CKD)

**Clinical Development**

**86,645** Participants enrolled in the **123 clinical trials** WW evaluating Farxiga

**58%** of clinical trials started post FDA approval

**\$5.2B** Estimated R&D spend

**Active Programs**

Phase III
<ul style="list-style-type: none"> <li>Acute myocardial infarction</li> <li>COVID-19 treatment</li> <li>Liver cirrhosis</li> </ul>

**Investments in Trials by Study Start Date**

	Pre-approval	Post-approval
Trial Cost	\$2.0B	\$3.4B

**Patents and Exclusivity**

Expected loss of exclusivity	2025
Years on the market	9.6

**Other Drugs in Therapeutic Class**

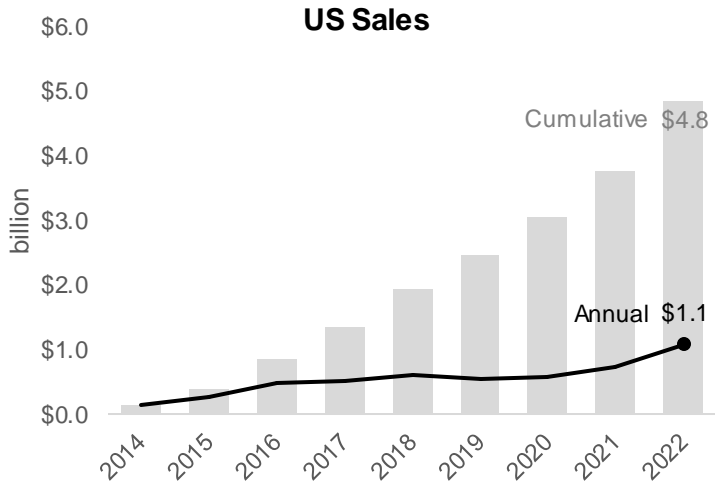
<b>Jardiance</b> Boehringer Ingelheim \$3.6B in US Sales, 2022	<b>Steglatro</b> Merck \$253M in US Sales, 2022	<b>Invokana</b> J&J \$193M in US Sales, 2022
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**Medicare Part D, 2021**

<b>\$1.4B</b> Total Gross Spending	<b>385,693</b> Total Beneficiaries
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**Portfolio Position**

<b>6%</b> of AstraZeneca's US Rx Sales, 2022	<b>#7</b> Sales Rank, 2022	<b>\$15.8</b> Global Lifetime Sales
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**Key Events**

**2014:** FDA approval and US launch for T2DM (1/8); AstraZeneca acquires BMS share of diabetes alliance for \$2.7bn upfront + \$1.7bn milestone payments

**2019:** FDA approves new indication to reduce risk of hospitalization for heart failure in patients with T2DM


**2020:** FDA approves new indication for treatment of heart failure in patients w/heart failure with reduced ejection fraction

**2021:** FDA approves new indication for CKD in patients at risk of progression with and without T2DM

# Imbruvica

(ibrutinib)

**AbbVie / Johnson & Johnson**



Originator: Celera / Pharmacyclics  
Capsules for oral use | small molecule

- Indications**
- ✓ Chronic lymphocytic leukemia/small lymphocytic lymphoma
  - ✓ Waldenstrom's macroglobulinemia (WM)
  - ✓ Graft vs host disease

**Clinical Development**

**18,088** Participants enrolled in the **127 clinical trials** WW evaluating Imbruvica

**76%** of clinical trials started post FDA approval

**\$1.4B** Estimated R&D spend

**Active Programs**

Phase III	Phase II		Phase I
<ul style="list-style-type: none"> <li>Acute myeloid leukaemia</li> <li>Acute lymphocytic leukaemia</li> </ul>	<ul style="list-style-type: none"> <li>Hairy cell leukaemia</li> <li>Gastro-intestinal adenocarcinoma</li> </ul>	<ul style="list-style-type: none"> <li>Multiple myeloma</li> <li>Breast cancer</li> <li>Solid tumor indications</li> <li>Melanoma</li> </ul>	<ul style="list-style-type: none"> <li>Renal cell carcinoma</li> <li>Bladder cancer</li> <li>Head &amp; neck cancers</li> </ul>
			<ul style="list-style-type: none"> <li>Chronic myelomonocytic leukaemia</li> <li>Myelodysplastic syndrome</li> </ul>

**Investments in Trials by Study Start Date**

Trial Cost	Pre-approval	Post-approval
	\$352M	\$1.2B

**Patents and Exclusivity**

<b>Expected loss of exclusivity</b>	2032
<b>Years on the market</b>	9.8

**Other drugs in same therapeutic class**

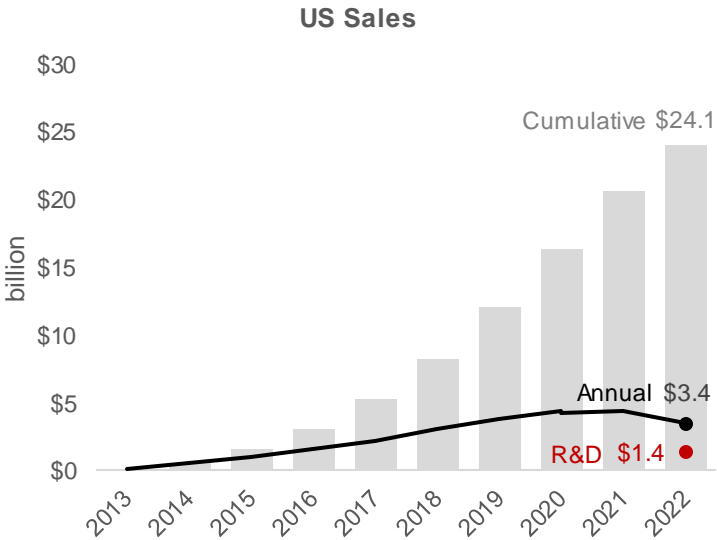
<p><b>Calquence</b> AstraZeneca \$1.7B in US Sales, 2022</p>	<p><b>Brukinsa</b> BeiGene \$390M in US Sales, 2022</p>
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**Medicare Part D, 2021**

<b>\$3.2B</b> Total Gross Spending	<b>26,044</b> Total Beneficiaries
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**Portfolio Position**

<b>7.5%</b> of AbbVie's US Rx Sales, 2022	<b>#3</b> Sales rank, 2022	<b>\$36.8B</b> Global Lifetime Sales
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**Key Events**

- 2006:** Pharmacyclics acquires NMEs from Celera for \$2mn + \$144mn milestone payments
- 2011:** Pharmacyclics and J&J agree to co-promote in the US
- 2013:** FDA approval and first launch (11/13) for mantle cell lymphoma
- 2014:** New indication for chronic lymphocytic leukemia
- 2015:** AbbVie acquires Pharmacyclics for \$21bn, J&J continues co-promotion; new indication for WM
- 2017:** FDA approves new indication for graft vs host disease
- 2022:** Two accelerated approval indications withdrawn



# Januvia

(sitagliptin phosphate)

**Merck** 

Tablets for oral use | small molecule

## Indications

- ✓ Januvia is a dipeptidyl peptidase-4 (DPP-4) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus

## Clinical Development

**48,237** Participants enrolled in the **93 clinical trials** WW evaluating Januvia

**75%** of clinical trials started post FDA approval\*

**\$5.3B** Estimated R&D spend

There are currently no active programs studying new indications for Januvia

### Investments in Trials by Study Start Date

	Pre-approval	Post-approval
<b>Trial Cost</b>	\$320M	\$5.0B

## Key Events

**2006:** First global launch (8/31); FDA approval (10/16) for Type 2 diabetes

## Patents and Exclusivity

<b>Expected loss of exclusivity</b>	2026
<b>Years on the market</b>	16.9

## Other Drugs in Therapeutic Class

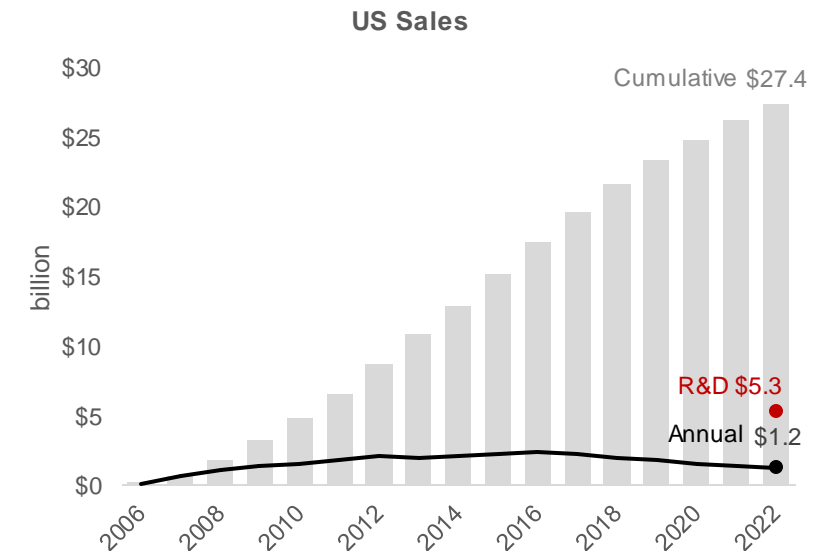
<b>Tradjenta</b> Boehringer Ingelheim \$862M in US Sales, 2022	<b>Nesina</b> Takeda \$93M in US Sales, 2022	<b>Onglyza</b> AstraZeneca \$76M in US Sales, 2022
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## Medicare Part D, 2021

<b>\$4.1B</b> Total Gross Spending	<b>934,542</b> Total Beneficiaries
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## Portfolio Position

<b>5%</b> of Merck's US Rx Sales, 2022	<b>#4</b> Sales Rank, 2022	<b>\$54.1B</b> Global Lifetime Sales
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\*Historical data on clinical trials and R&D costs may be limited because FDA approval for this drug preceded clinical trial reporting requirements

# Jardiance

(empagliflozin)

## Boehringer Ingelheim/ Eli Lilly



Originator: Boehringer Ingelheim  
Tablets for oral use | small molecule

### Indications

- ✓ Reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure, established cardiovascular disease, and Type 2 diabetes.
- ✓ Adjunct to diet and exercise to improve glycemic control in adults with T2DM.

### Clinical Development

**56,265** Participants enrolled in the **100 clinical trials** WW evaluating Jardiance

**40%** of clinical trials started post FDA approval

**\$3.5B** Estimated R&D spend

#### Active Programs

##### Phase III

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>• General cardiovascular indications</li> <li>• Acute myocardial infarction</li> </ul> | <ul style="list-style-type: none"> <li>• Diabetes, type 1</li> <li>• Acute decompensated heart failure</li> </ul> |
|---|---|

#### Investments in Trials by Study Start Date

	Pre-approval	Post-approval
Trial Cost	\$2.2B	\$1.6B

### Patents and Exclusivity

Expected loss of exclusivity	2028
Years on the market	9.1

### Other Drugs in Therapeutic Class

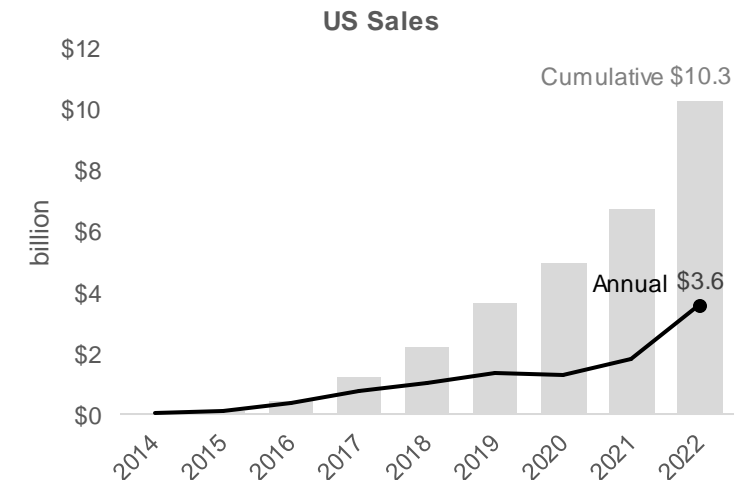
<b>Farxiga</b> AstraZeneca \$1.1B in US Sales, 2022	<b>Steglaro</b> Merck \$253M in US Sales, 2022	<b>Invokana</b> J&J \$193M in US Sales, 2022
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### Medicare Part D, 2021

<b>\$3.7B</b>	<b>884,516</b>
Total Gross Spending	Total Beneficiaries

### Portfolio Position

<b>33%</b>	<b>#1</b>	<b>\$18.3B</b>
of Boehringer Ingelheim's US Rx Sales, 2022	Sales Rank, 2022	Global Lifetime Sales



### Key Events

**2011:** Eli Lilly & Boehringer Ingelheim form alliance to jointly develop & commercialize drug for global market


**2014:** FDA approval and first worldwide launch in US (8/1) for Type 2 diabetes

**2021:** FDA approves new indication for chronic heart failure

# Novolog

(insulin aspart)

**Novo Nordisk**



Biologic | large molecule

### Indications

- ✓ Novolog is an insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus.

### Clinical Development

Historical data on clinical development is limited because FDA approval for this drug preceded clinical trial reporting requirements.

### Patents and Exclusivity

Expected loss of exclusivity	2014
Years on the market	23.2

### Other Drugs in Therapeutic Class

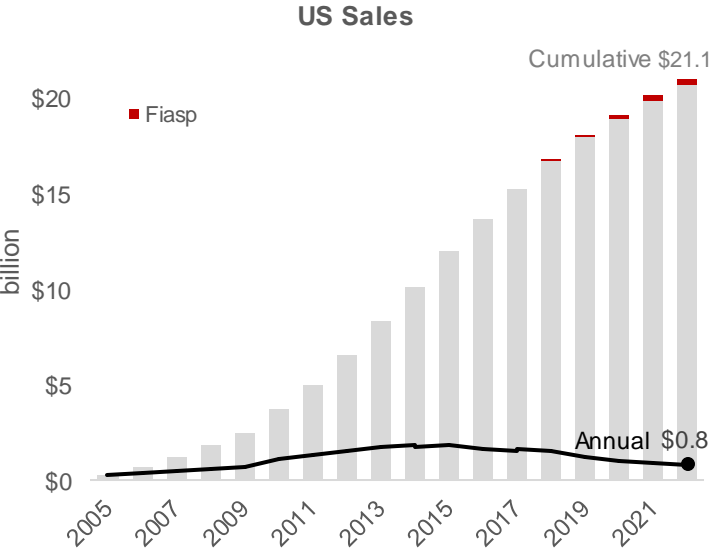
<b>Humalog</b> Eli Lilly \$1.2B in US Sales, 2022	<b>Humulin R</b> Eli Lilly \$730M in US Sales, 2022	<b>Admelog</b> Sanofi \$136M in US Sales, 2022
<b>Afrezza</b> MannKind \$43M in US Sales, 2022	<b>Apidra</b> Sanofi \$30M in US Sales, 2022	

### Medicare Part D, 2021

<b>\$2.5B</b> Total Spending Novolog, Fiasp, Insulin Aspart packages	<b>874,025</b> Total Beneficiaries
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### Portfolio Position

<b>7%</b> of Novo Nordisk's US Rx Sales, 2022	<b>#4</b> Sales Rank, 2022	<b>\$42.8B</b> Global Lifetime Sales
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### Key Events

**1999:** First worldwide launch (9/30)

**2000:** FDA approval for Type 1 & 2 diabetes (6/7)

**2018:** First US launch for Fiasp (2/5)


**2020:** Novo Nordisk introduces authorized generic

**2024:** Novo Nordisk announces up to 75% price cut

# Stelara

(ustekinumab)

**Johnson & Johnson**



Originator: Centocor  
Injection | large molecule

**Indications**

- ✓ Moderate to severe plaque psoriasis (Ps)
- ✓ Active psoriatic arthritis (PsA)
- ✓ Moderately to severely active Crohn's disease
- ✓ Moderately to severely active ulcerative colitis

**Clinical Development**

**18,282** Participants enrolled in the **61 clinical trials** WW evaluating Stelara

**84%** of clinical trials started post FDA approval      **\$2.1B** Estimated R&D spend

**Active Programs**

Phase III
<ul style="list-style-type: none"> <li>Juvenile idiopathic arthritis</li> <li>Type 1 diabetes</li> </ul>

**Investments in Trials by Study Start Date**

	Pre-approval	Post-approval
<b>Trial Cost</b>	\$616M	\$1.6B

**Patents and Exclusivity**

<b>Expected loss of exclusivity</b>	2025
<b>Years on the market</b>	13.9

**Other Drugs in Therapeutic Class**

<p><b>Dupixent</b> Sanofi \$6.8B in US Sales, 2022</p>	<p><b>Cosentyx</b> Novartis \$2.8B in US Sales, 2022</p>	<p><b>Taltz</b> Eli Lilly \$1.7B in US Sales, 2022</p>
<p><b>Actemra</b> Roche \$1.3B in US Sales, 2022</p>	<p><b>Ilaris</b> Novartis \$570M in US Sales, 2022</p>	

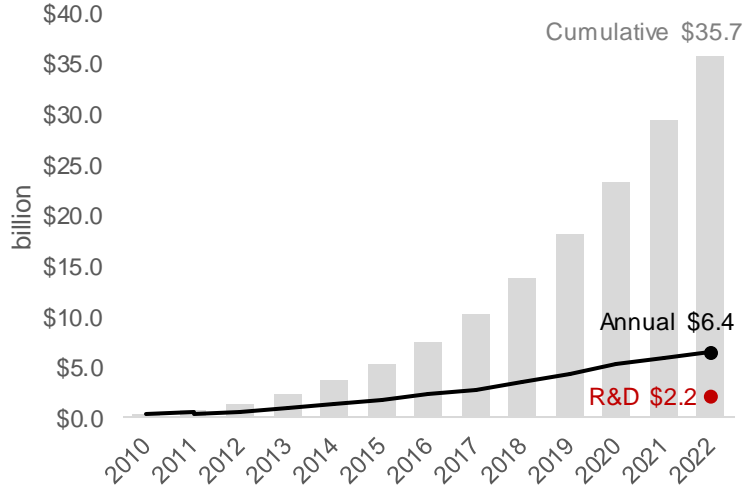
**Medicare Part D, 2021**

**\$1.6B** Total Gross Spending      **16,156** Total Beneficiaries

**Portfolio Position**

**22%** of J&J's US Rx Sales, 2022      **#1** Sales Rank, 2022      **\$54.8B** Global Lifetime Sales

**US Sales**



**Key Events**

- 1999:** J&J acquires Centocor for \$4.9 billion in stock
- 2009:** FDA approval for psoriasis (9/25)
- 2013:** New indication for PsA
- 2016:** New indication for Crohn's disease
- 2017:** New indication for Ps
- 2019:** New indication for ulcerative colitis
- 2020:** New indication for pediatric psoriasis
- 2023:** J&J settles patent litigation w/Amgen, Alvotect, and Teva to permit biosimilar entry by 1/1/2025

# Xarelto

(rivaroxaban)

## Bayer / Johnson & Johnson



Originator: Bayer

Tablets for oral use | small molecule

## Indications

- ✓ Reduce risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation
- ✓ Reduce risk of major thrombotic vascular events in patients with peripheral artery disease
- ✓ Treatment of deep vein thrombosis, pulmonary embolism, and venous thromboembolism

## Clinical Development

**231,125** Participants enrolled in the **81 clinical trials** WW evaluating Xarelto

**64%** of clinical trials started post FDA approval

**\$7.8B** Estimated R&D spend

### Active Trials

Phase III
<ul style="list-style-type: none"> <li>• COVID-19 treatment</li> <li>• Chronic kidney disease</li> <li>• Chronic heart failure</li> </ul>

### Investments in Trials by Study Start Date

	Pre-approval	Post-approval
Trial Cost	\$3.4B	\$4.5B

## Patents and Exclusivity

**Expected loss of exclusivity** 2025

**Years on the market** 15

## Other Drugs in Therapeutic Class

**Eliquis**  
Bristol-Myers Squibb  
\$7.8B in US Sales, 2022

**Lixiana**  
Daiichi Sankyo  
\$23M in US Sales, 2022

## Medicare Part D, 2021

**\$5.2B**

Total Gross Spending

**1,258,010**

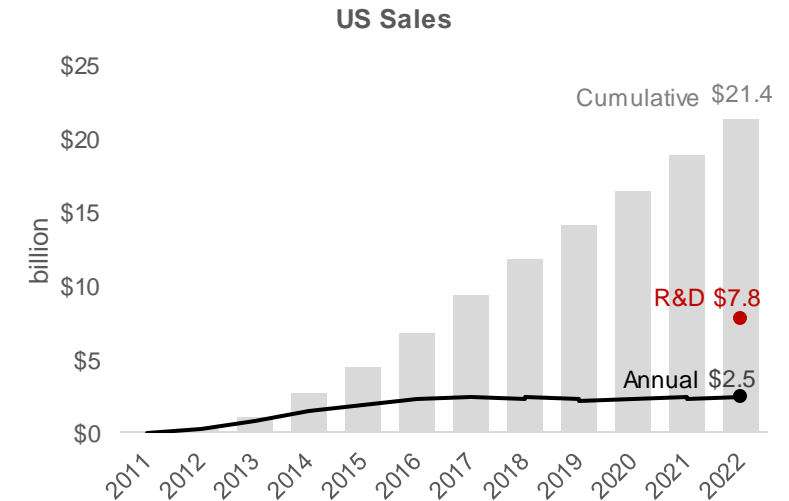
Total Beneficiaries

## Portfolio Position

**8.7%**  
of J&J's US Rx Sales, 2022

**#3**  
Sales Rank, 2022

**\$54.3B**  
Global Lifetime Sales



## Key Events

**2005:** Bayer and J&J agree to co-develop, with J&J managing US markets and Bayer ex-US

**2008:** First launch ex-US (9/16)

**2011:** FDA approval for stroke prophylaxis secondary to atrial fibrillation, deep vein thrombosis, and pulmonary embolism

**2014:** FDA approves new indication for thrombosis

**2018:** FDA approves new indication for peripheral vascular disease

## Sources

Indications: [Drugs@FDA](#); or manufacturer website.

Key Events: [Evaluate](#) Pharma and press releases.

Financial and clinical trial data: [Evaluate](#) Pharma and Omnium, accessed August 25, 2023.

Medicare Part D: Medicare spending [dashboard](#), accessed August 25, 2023.

## Definitions and Methods

Key events: Dates of key mergers and acquisitions, approvals and launch, and approvals for new indications were obtained from Evaluate Pharma and press releases.

Company's US Rx sales: Total US sales for all prescription drugs in the manufacturer's portfolio in 2022 by total US sales for drug of interest.

Global sales: Sum of worldwide (WW) sales from launch to 2022.

Clinical development: Active programs are based on [clinicaltrials.gov](#) status and company disclosures, sourced from [Evaluate](#).

Clinical trials: Phase I-III clinical trials are included if they are registered on [clinicaltrials.gov](#) and the company marketing the product in the main comparator arm is listed as a study sponsor or collaborator.

Phase IV studies are similarly classified and included for top 20 companies (based on R&D spending). Sourced from [Evaluate](#) Omnium.

Clinical trial costs: Annualized estimates are based on R&D spending disclosures from company 10-Ks, where available, to 2022. If spending figures are not disclosed, costs are imputed from disclosures made by other companies for similar technologies and indications. Imputed costs are further adjusted for geography, trial length, and any other company-reported product-level spend. Sourced from [Evaluate](#) Omnium.

Therapeutic class: Based on 2023 EphMRA ATC codes.

## Therapeutic Class

Product	EphMRA ATC	Definition
Eliquis	B1F	Direct factor Xa inhibitor
Enbrel	L4B	Anti-TNF products
Entresto	C9D9	Angiotensin-II antagonist combinations with other drugs
Farxiga	A10P1	SGLT2 inhibitor antidiabetics, plain
Imbruvica	L1H6	Protein kinase inhibitor antineoplastics, BTK
Januvia	A10N1	DPP-IV inhibitor antidiabetics, plain
Jardiance	A10P1	SGLT2 inhibitor antidiabetics, plain
Novolog	A10C1	Human insulins & analogues, fast-acting
Stelara	L4C	Interleukin inhibitors
Xarelto	B1F	Direct factor Xa inhibitor

## Glossary

IRA – Inflation Reduction Act

MFP – maximum fair price

NME – new molecular entity

WW – worldwide

## Estimating Clinical Trial Costs

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Data on clinical trials and costs of clinical development are from Evaluate. Evaluate identifies commercial clinical trials by identifying Phase I-IV studies on clinical trials.gov that list the manufacturer of the drug in the main comparator arm of the trial as a sponsor or collaborator. The number of patients enrolled in such clinical trials are then estimated for each product for any years between 2007-2022 based on the start date of the clinical trial, enrollment accrual, and duration of the study.

Separately, Evaluate maintains a database of product-specific R&D spending as reported by 433 companies in their 10-K filings, which includes approximately 1,600 compounds. These data span from 2007-2021.

Using these two sources, Evaluate calculates total Phase II-IV R&D spending for products with available 10-K spending data across active years, as well as the total number of patients enrolled in its clinical trials. An average cost per patient (CPP) of clinical development for the product is calculated by dividing total R&D spending by total number of patients.

However, not all manufacturers report product-level R&D spending. In these instances, Evaluate imputes an average cost per patient using other companies' spending on comparable products and clinical trials as benchmarks. The benchmarks are selected according to the following algorithm:

1. If available, use CPP averages from trials for drugs of the same technology and developed for the same indication (EphMRA level 3),
2. If 1 isn't available, use CPP averages from trials for drugs of the same technology (e.g., small molecule, biologic, gene therapy, etc.) and developed for similar indications (EphMRA level 1),
3. If 2 isn't available, use CPP averages from trials for drugs based on the same technology

The closest matching benchmark is then multiplied by the number of patients enrolled in clinical trials for the drug. This estimate is adjusted based on differences between the trials used to calculate the benchmark and the trials for the product, including different geographies and duration of the trials. In addition, adjustments are made for any company-reported disclosures related to R&D spending.

In addition, Evaluate further adjusts the estimates for individual products to reflect their share of the company's R&D spend for the companies included in our analysis.

Phase I spending estimates are based on coefficients from a regression analysis estimating fixed and variable costs for Phase I clinical trials.

We conducted sensitivity analyses to assess the effect of variability in benchmarks and later phase spending on our analysis. We found that imputing costs using different cost benchmarks and excluding Phase IV trials and did not significantly change the magnitude or direction of our estimates.