# MARKET WATCH

## Imbruvica

### BACKGROUND

- Imbruvica is an oral small molecule Bruton's tyrosine kinase inhibitor that was initially developed by the biopharmaceutical company Pharmacyclics.
- Pharmacyclics was purchased by AbbVie in 2015 for $21 billion, and is now a wholly owned subsidiary of AbbVie. As part of the acquisition, AbbVie inherited a co-development partnership with Johnson & Johnson (J&J) that gave the two companies co-exclusive rights to commercialize the drug in the U.S. (with AbbVie as the principal) and J&J exclusive rights to sell the drug outside the U.S.
- Since its launch, Imbruvica has been a blockbuster commercial success, generating over $15 billion for the two companies in just five years, fueled by label expansions and a 57%[1] price increase price to an annual list price of $174,000[2].
- Imbruvica is now AbbVie's second-bestselling product behind Humira, which is currently the top-selling drug in the world.[3]

### FDA APPROVALS

**Approved Formulations**

*Capsules:* 140mg (Feb 2013), 70mg (Dec 2017)

*Tablets:* 140mg, 280mg, 420mg, 560mg (Feb 2018)

**Current Approved Indications**

Mantle Cell Lymphoma (Nov 2013)

Chronic Lymphocytic Leukemia (Feb 2014)

Marginal Zone Lymphoma (Jan 2017)

Waldenstrom's Macroglobulinemia (Jan 2015)

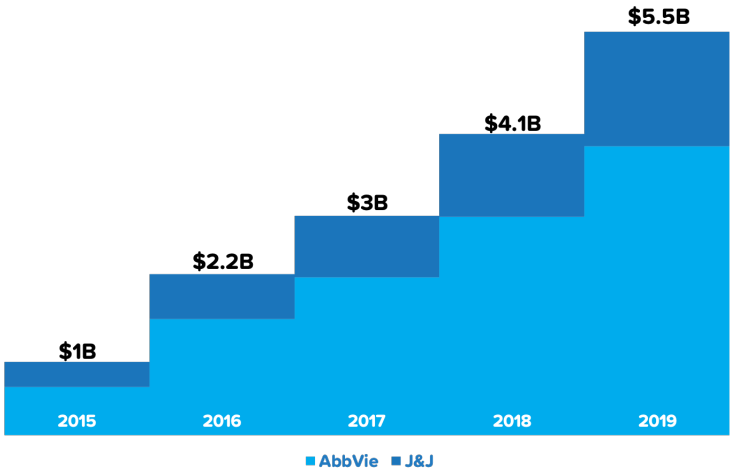
Small Lymphocytic Lymphoma (May 2016)

Chronic Graft-Versus-Host (Aug 2017)

[1] Based on Average Wholesale Price (AWP) for 140mg capsule, 120 per package, from Jan 1, 2014 to Jan 1. 2019.
[2] For the most widely used 140mg oral capsule, 90 capsule (one-month supply). https://www.drugs.com/price-guide/imbruvica
[3] https://www.fiercepharma.com/special-report/7-imbruvica

## Revenue and Outlook

**Revenue for Imbruvica in the U.S.**




- Total net spending in the U.S. has exceeded $15 billion in the six years since its approval, with average annual growth of 56% in the past four years.[4]
- By 2024, Imbruvica is estimated to become the fourth highest grossing drug in the U.S. with annual revenues of nearly nine billion dollars.[5]

## Clinical Strategy and Development

- AbbVie has aggressively pursued new indications for Imbruvica. As of Feb 2020, there are 10 different FDA approvals for six different indications for the drug. This label expansion strategy is a driver of additional revenue for the drug.
- To further expand the Imbruvica franchise, it is being tested and developed in phase II or III clinical trials for sixteen additional indications.[6]

### PIPELINE

Phase II/III clinical trials of Imbruvica

*Lymphomas*

1. Non-Hodgkin's Lymphoma
2. Mature B-cell Non-Hodgkin Lymphoma
3. Diffuse Large B-Cell Lymphoma
4. Follicular Lymphoma
5. CNS Lymphoma

*Leukemias*

6. Lymphoblastic Leukemia
7. Acute Myeloid Leukemia
8. T-Cell Prolymphocytic Leukemia

*Other Cancers*

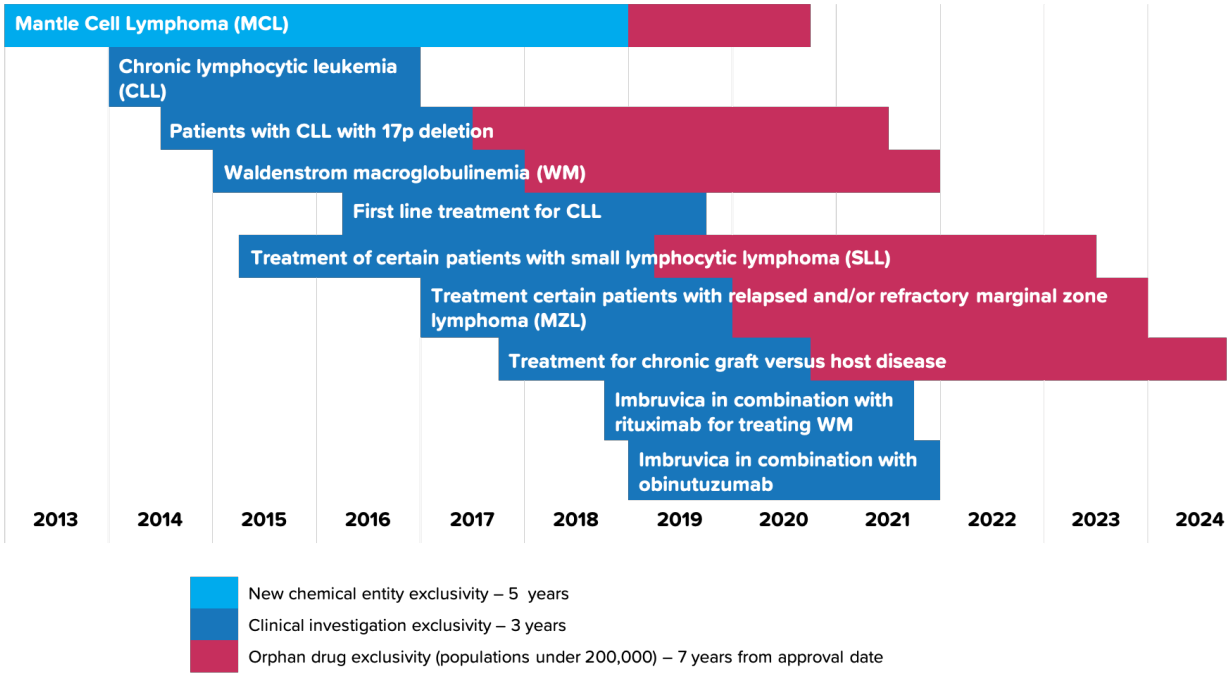
9. Multiple Myeloma
10. Esophageal cancer
11. Head and Neck Cancer
12. Bladder cancer
13. Stomach cancer
14. Colorectal Cancer
15. Breast Cancer
16. Lung Cancer
17. Kidney Cancer
18. Prostate Cancer

[4] From an analysis of the annual and quarterly reports of AbbVie and J&J from 2014-2019. Actual figures for Q4 2019 are not yet available and are estimates.
[5] EvaluatePharma World Preview Report. Table 14: Top 10 Selling Products in the USA in 2024. May, 2019.
[6] Imbruvica is being tested by industry as a standalone or combination therapy in phase II or III clinical trials for diseases that are *not* already FDA-approved for the drug. A total of 26 separate trials and 16 distinct disease areas was found. Data available at ClinicalTrials.gov database.

# Non-Patent Exclusivities

In addition to patent exclusivity, Imbruvica is protected by marketing exclusivities given by the FDA. Unlike patents, these marketing exclusivities cannot be litigated and are a guaranteed period of protection free from any generic competition. Non-patent exclusivities for the current indications for Imbruvica have a duration of 11 years.

- Imbruvica's first FDA exclusivity was the 5-year new chemical entity marketing exclusivity for mantle cell lymphoma in 2013. This marketing exclusivity expired in 2018.
- Eight 3-year clinical investigation exclusivities (CIEs) have been granted for Imbruvica in relation to each subsequent approved indication. Five CIEs have expired; three CIEs are currently in force and expire between August 2020 and January 2022.
- Orphan Drug Exclusivities (ODE) for Imbruvica, which are given for products that treat indications affecting fewer than 200,000 people, have been granted for eight indications and expire between January 2020 and August 2024.




# Litigation Summary

### Orange Book Patents

- As of February 2020, there are a total of 31 total Orange Book patents listed for Imbruvica.
- 13 patents relate to the main compound, the remaining 18 cover the indications Imbruvica can be used for and how it is formulated (a tablet or a capsule, for example).

**Litigation**

The following companies filed Abbreviated New Drug Applications (ANDA) to market generic versions of Imbruvica in capsule or tablet form for the different indications and entered into litigation with Pharmacyclics LLC:

1. Alvogen Pine Brook LLC
2. Cadila Healthcare Limited
3. Cipla Limited
4. Cipla USA Inc.
5. Fresenius Kabi USA, LLC
6. Fresenius Kabi USA, Inc.
7. Fresenius Kabi Oncology Ltd
8. Hetero Laboratories
9. Lek Pharmaceuticals D.D.
10. Natco Pharma Limited
11. Sandoz Inc
12. Shilpa Medicare Limited
13. Sun Pharma Global FZE
14. Sun Pharmaceutical Industries Ltd.
15. Teva Pharmaceuticals USA, Inc.
16. Teva Pharmaceutical Industries Ltd.
17. Zydus Worldwide DMCC

**Settlements**

In 2019, Pharmacyclics and Janssen Biotech entered into confidential settlements with three of the generic challengers: Teva, Hetero, and Shilpa.

**Inter Partes Review (IPR)**

Sandoz filed an IPR petition with the Patent Trial and Appeals Board against Patent No. 9,795,604, which covers the use of Imbruvica to treat chronic graft versus host disease. The IPR petition was instituted and a hearing is scheduled for June 2020.

**Global**

- *Europe:* Generics UK revoked European patent EP2529622 relating to Imbruvica.
- *India:* In December 2019, a generic form of Imbruvica was launched in India by Natco amidst ongoing litigation and patent challenges for invalidating the main compound patent. In March 2020, granted Indian Patent No. 262968 protecting the main compound was revoked by the Indian Patent Office on the ground that it was an obvious invention.

**Overpatented, Overpriced: Imbruvica's Patent Wall**, and supplementary material on the drug and its patents, is available at **i-mak.org/imbruvica**