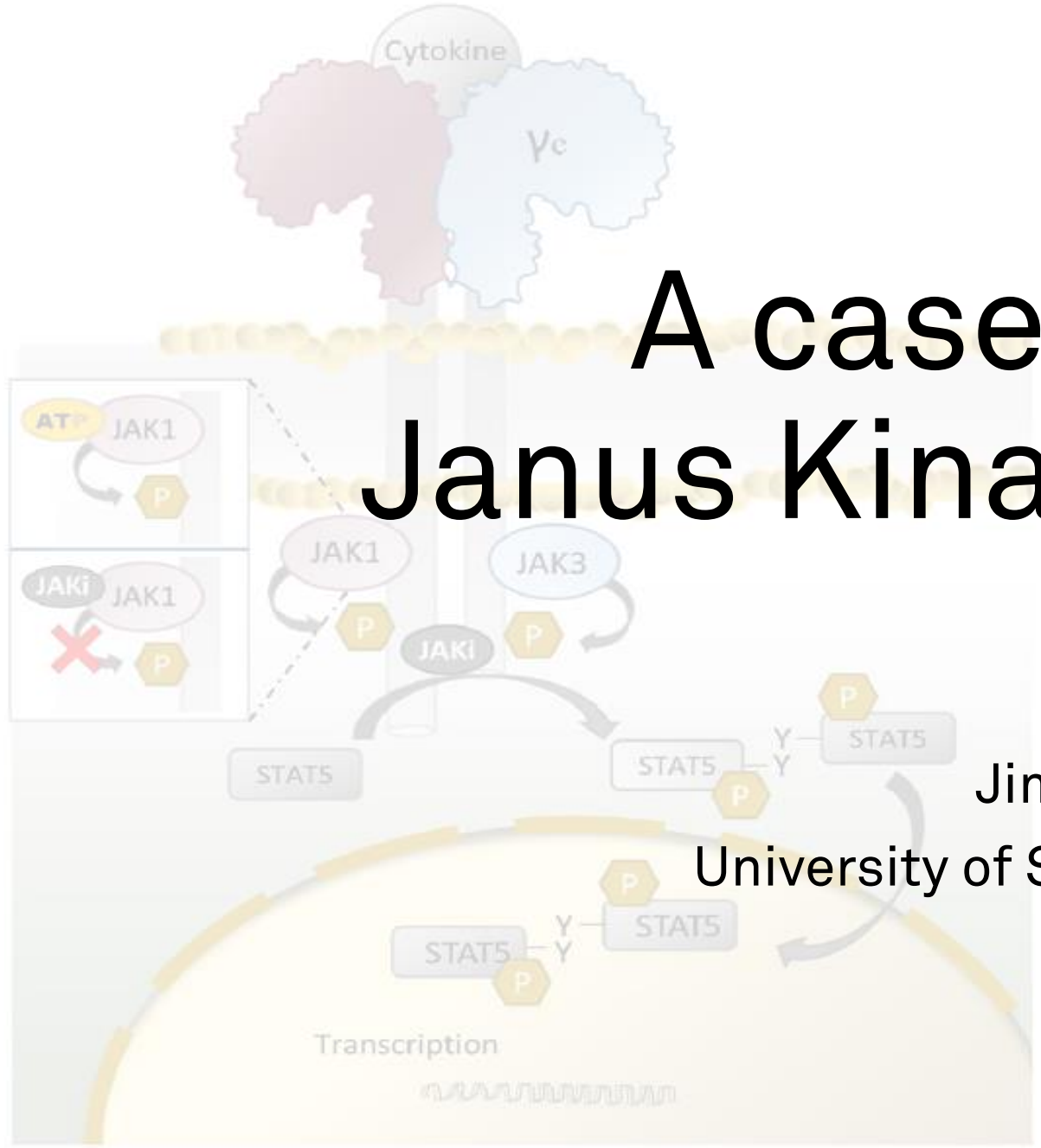


A case study in Janus Kinase Inhibitors

Jimmy Joy

University of Southern California

JAK Inhibition is a Therapeutic Strategy for Inflammatory Diseases

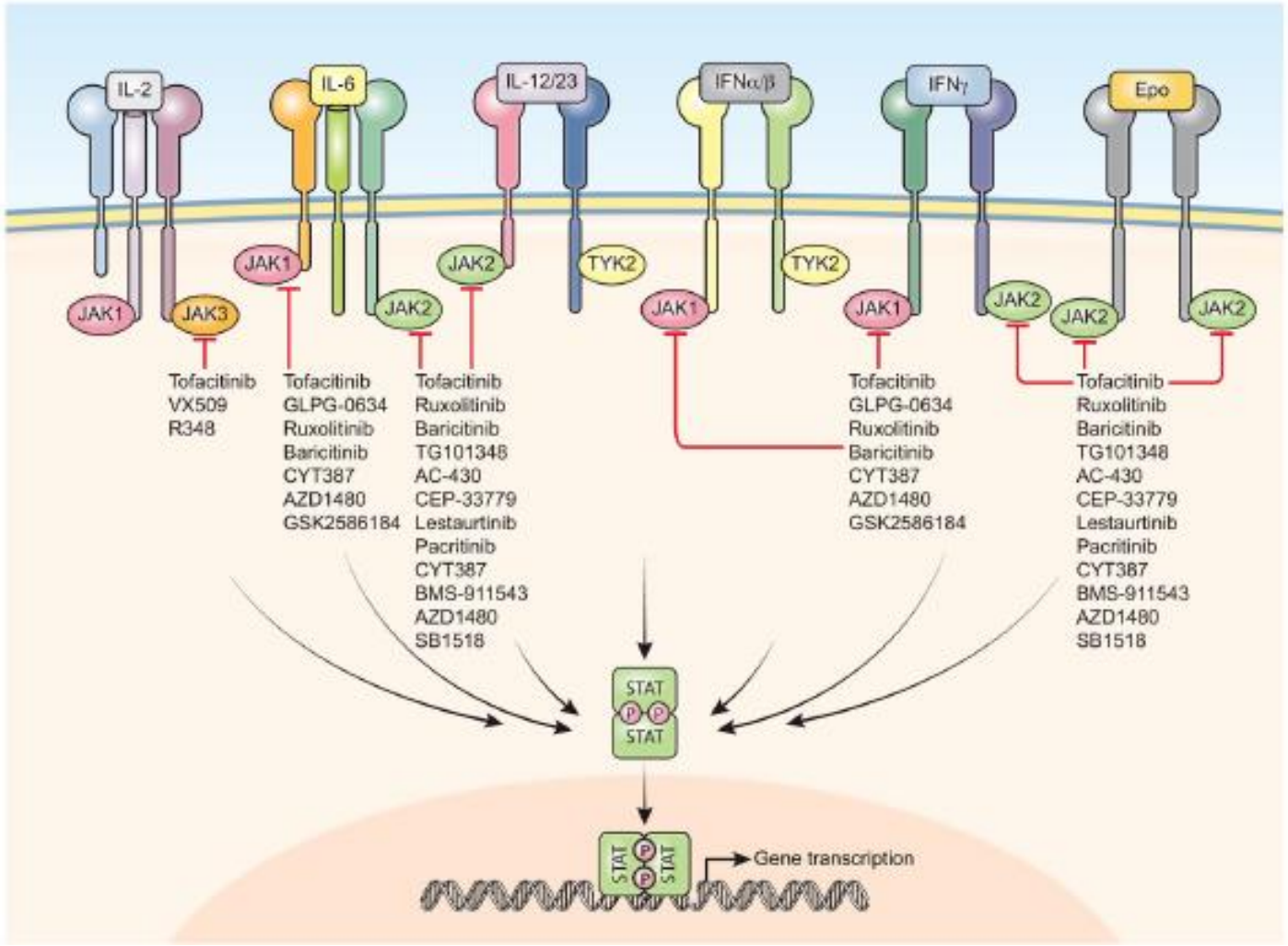


Chart 1. Inhibitors that act on the JAK – STAT pathway

- Janus Kinase – Signal Transducer and Activator of Transcription (*JAK-STAT*) pathway communicates signals from outside the cell to the nucleus to activate transcription of genes
- JAK-STAT pathway is implicated in inflammatory and autoimmune diseases and malignancies
- Tofacitinib, Ruxolitinib and Baricitinib and first generation JAK-inhibitors block one or more of JAK1, 2, 3 and TYK2
- Second generation JAK-inhibitors act selectively on single JAK and have less adverse effects

Selective Janus kinase inhibitors come of age, *Nature Reviews Rheumatology* 2019

Commercial Success increases with Therapeutic Value

- **40%** How has the drug performed to date?
- **20%** How is the drug doing compared to expectations?
- **40%** How will the drug perform in the future?

- **60%** How did the drug compare to standard of care at launch?
- **20%** How big was the unmet need?
- **20%** How novel was the drug?

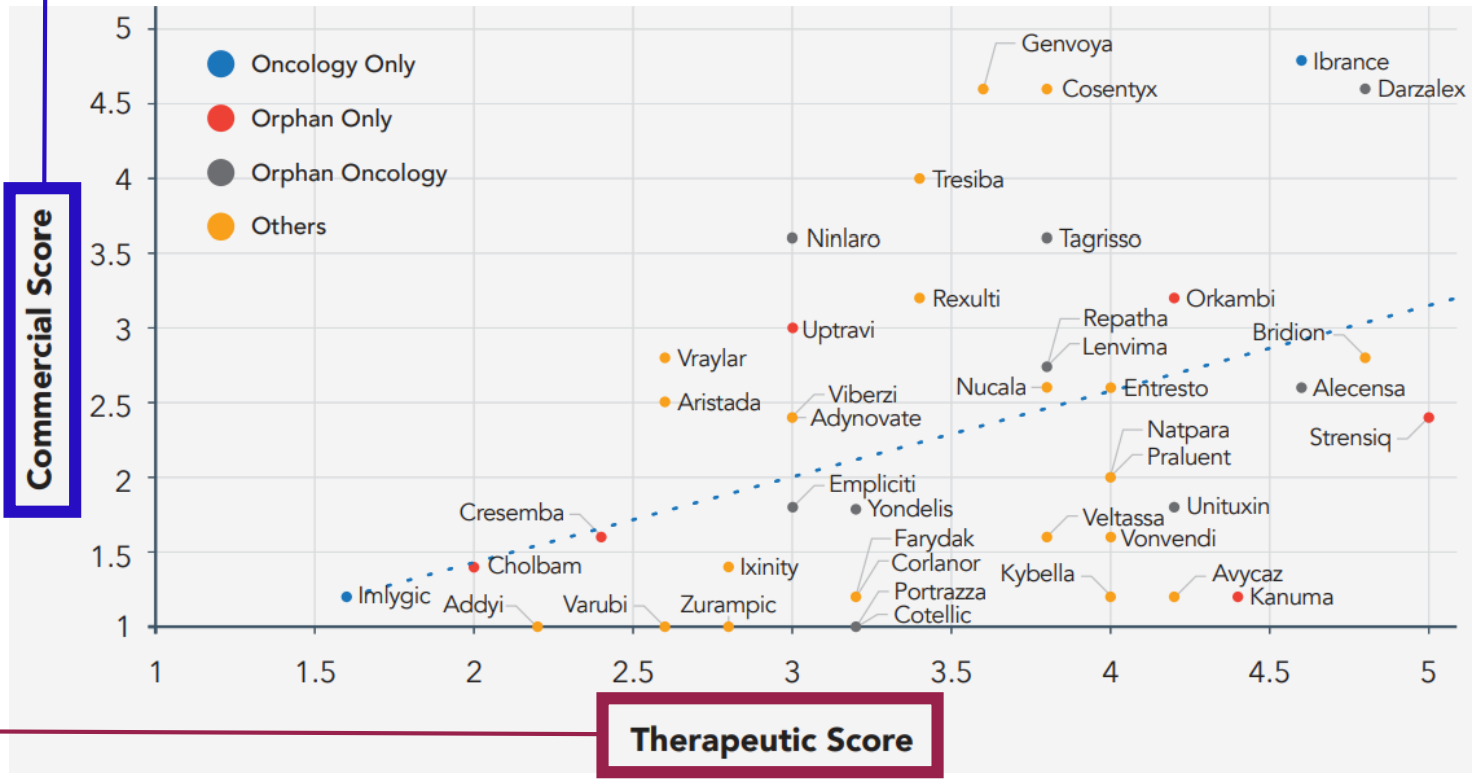


Chart 2. Trinity's rankings of 2015 drug introductions

Trinity Partners, Trinity Drug Index **2016, 2017**, and **2018**; What drives success for specialty pharmaceuticals?, *Nature Reviews Drug Discovery* **2008**

Differentiation relative to standard of care is the primary driver of success

How did the drug compare to standard of care at launch?

How big was the unmet need?

How novel was the drug?

5	4	3	2	1
Ruxolitinib	Baricitinib	Itacitinib	Tofacitinib	R348
Pacritinib	Cerdulatinib	Peficitinib	Lestaurtinib	
Fedratinib	Momelotinib	Gandotinib	BMS911543	
Filgotinib	Abrocitinib	PF06651600	INCB047986	
BMS986165	Upadacitinib	PF06700841	INCB52793	
	Decernotinib	SHR0302	PF06826647	
	Solcitinib			

Trinity Drug Index **2016, 2017**, and **2018**; What drives success for specialty pharmaceuticals?, *Nature Reviews Drug Discovery* **2008**

Market size at launch can be measured in terms of number of indications

How did the drug compare to standard of care at launch?

How big was the unmet need?

How novel was the drug?

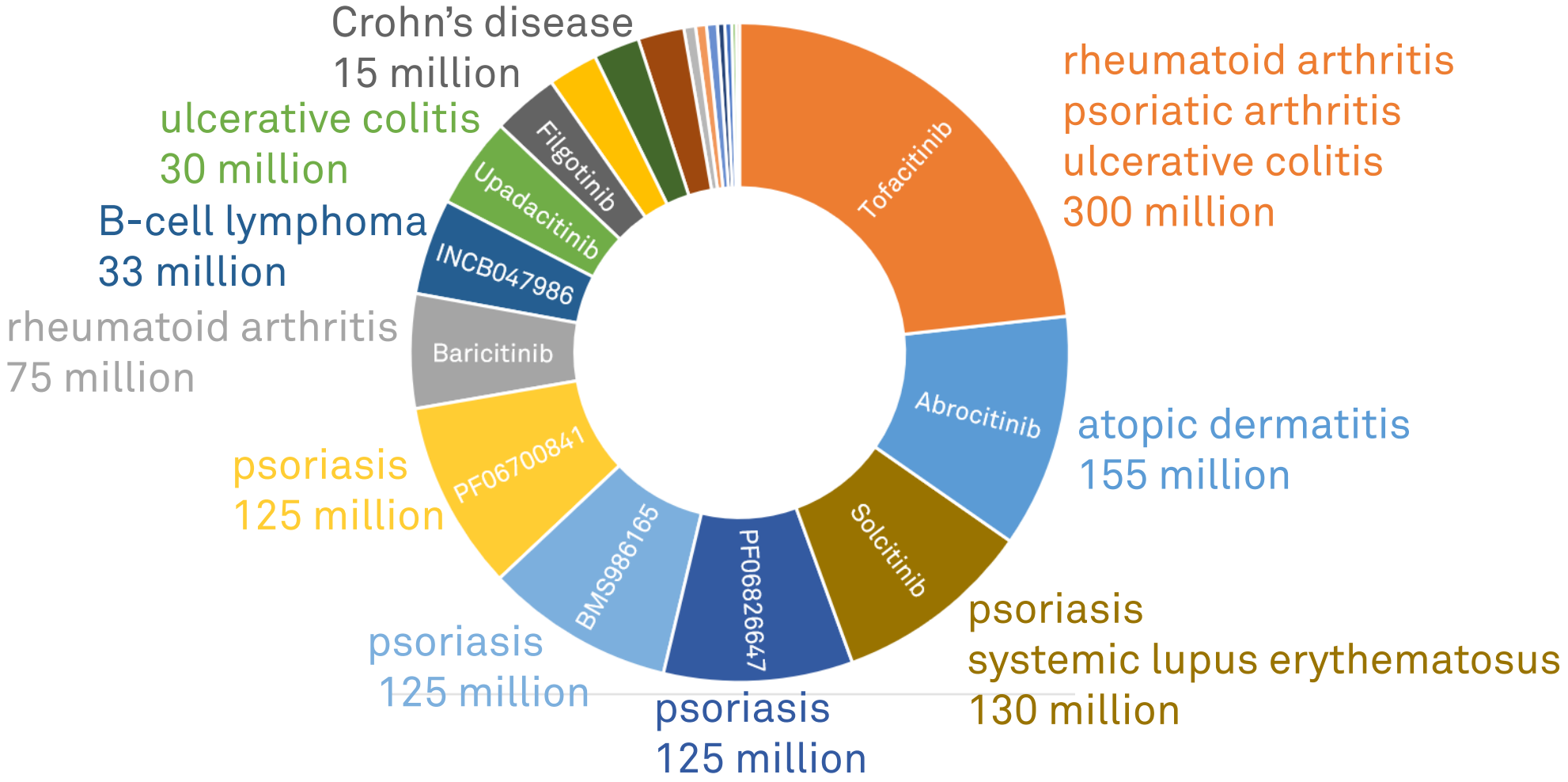


Chart 3. Quantifying the patient pool for major indications covered by JAK inhibitors

Data sourced from *EvaluatePharma*

JAK-specific inhibition is a novel mechanism of action

How did the drug compare to standard of care at launch?

How big was the unmet need?

How novel was the drug?

JAK inhibitor	Number of Janus Kinase enzymes inhibited	Score
Pacritinib, Abrocitinib, Upadacitinib, Fedratinib, Decernotinib, R348, BMS911543, Solcitinib, Itacitinib, INCB52793, PF06651600, BMS986165, PF06826647	1	5
Baricitinib, Lestaurtinib, Filgotinib, PF06700841	2	4
Ruxolitinib, Tofacitinib, Momelotinib, INCB047986, Peficitinib, Gandotinib, SHR0302	3	3
Cerdulatinib	4	2

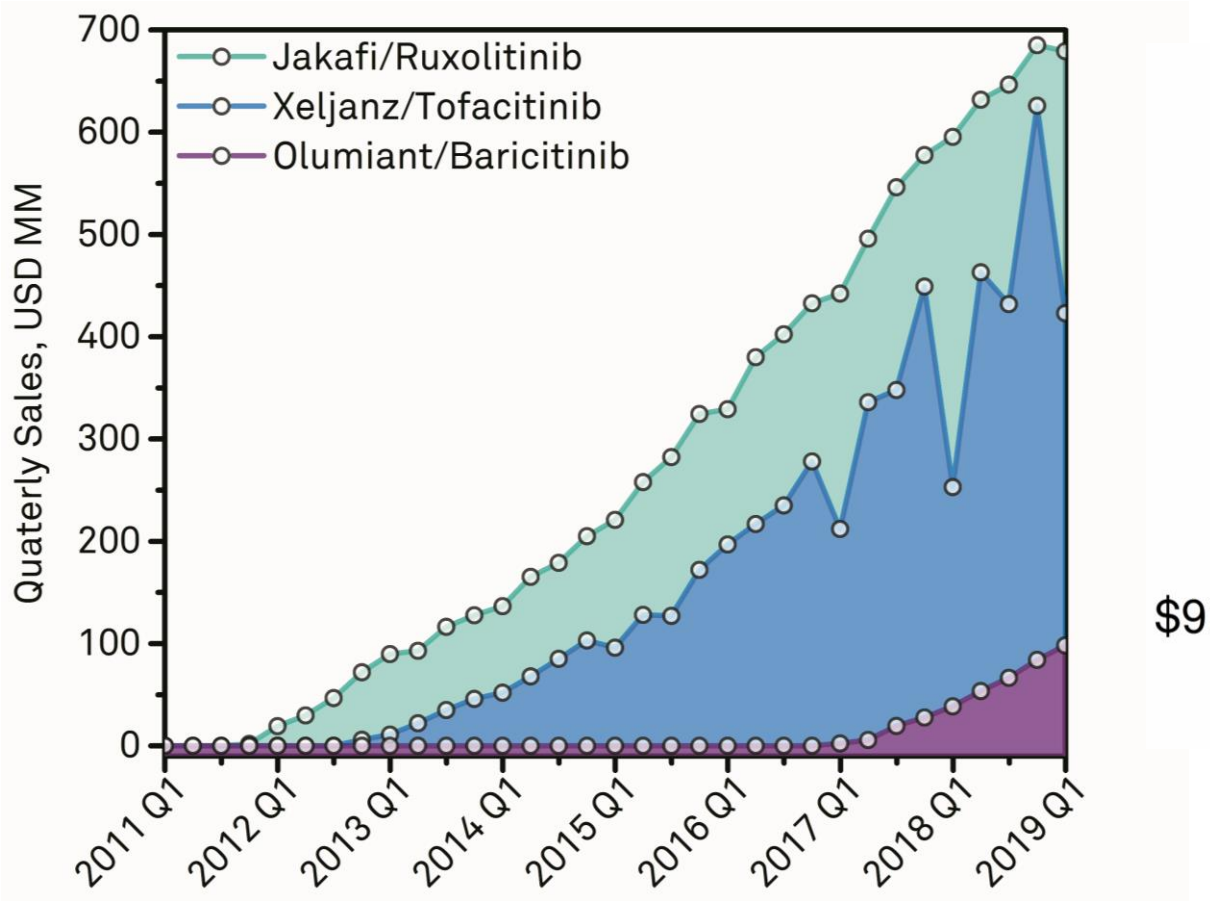
Sourced from *clinicaltrials.gov*, company websites

Cumulative sales is a measure of performance till date

How has the drug performed to date?

How is the drug doing compared to expectations?

How will the drug perform in the future?



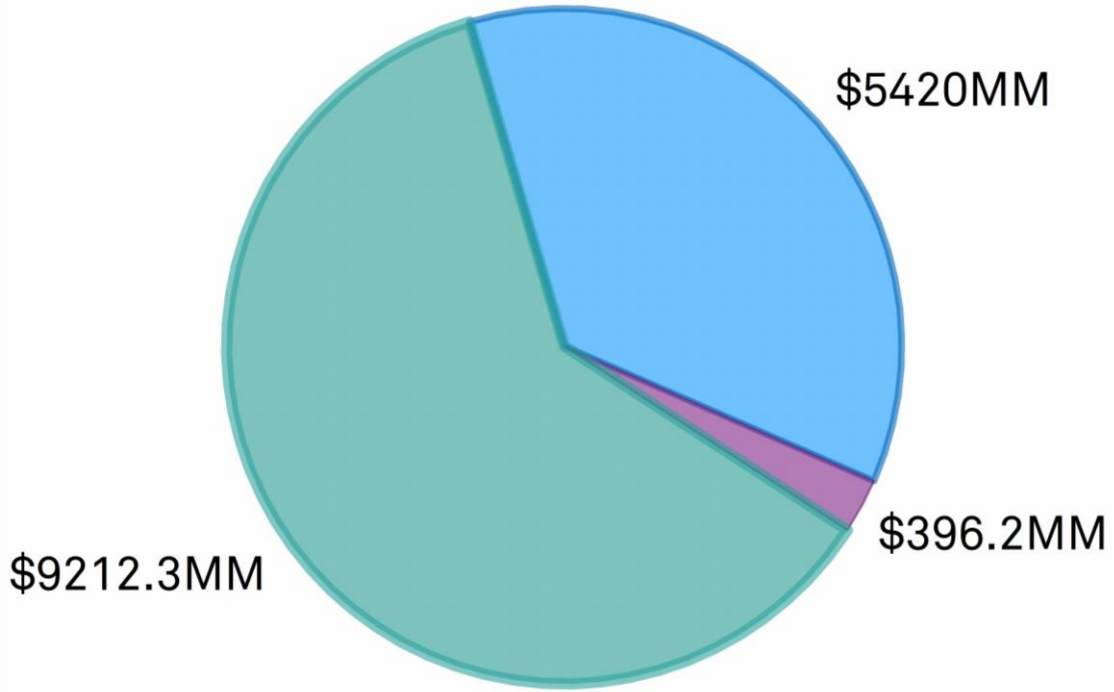


Chart 4. Quarterly sales revenue from Jakafi (Incyte, Novartis), Xeljanz (Pfizer) and Olumiant (Incyte, Eli Lilly) [left] and their cumulative sales till 2018 [right]

Quarterly sales figures obtained from SEC filings, Incyte, Pfizer, Novartis, Eli Lilly **2011-2018**

Deviation from forecasted sales can be used to compare expectations

How has the drug performed to date? | **How is the drug doing compared to expectations?** | How will the drug perform in the future?

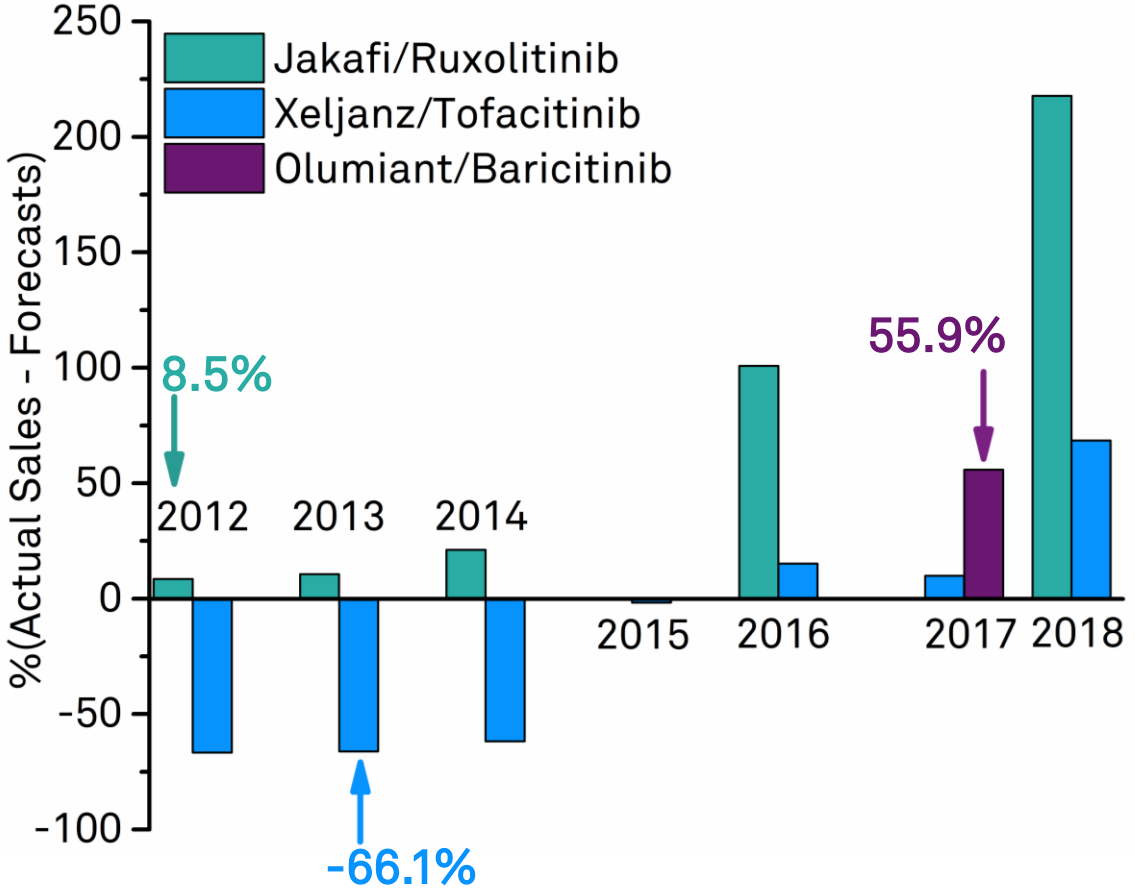


Chart 5. Per cent difference of actual sales from equity analyst forecasts for Jakafi, Xeljanz and Olumiant since launch year

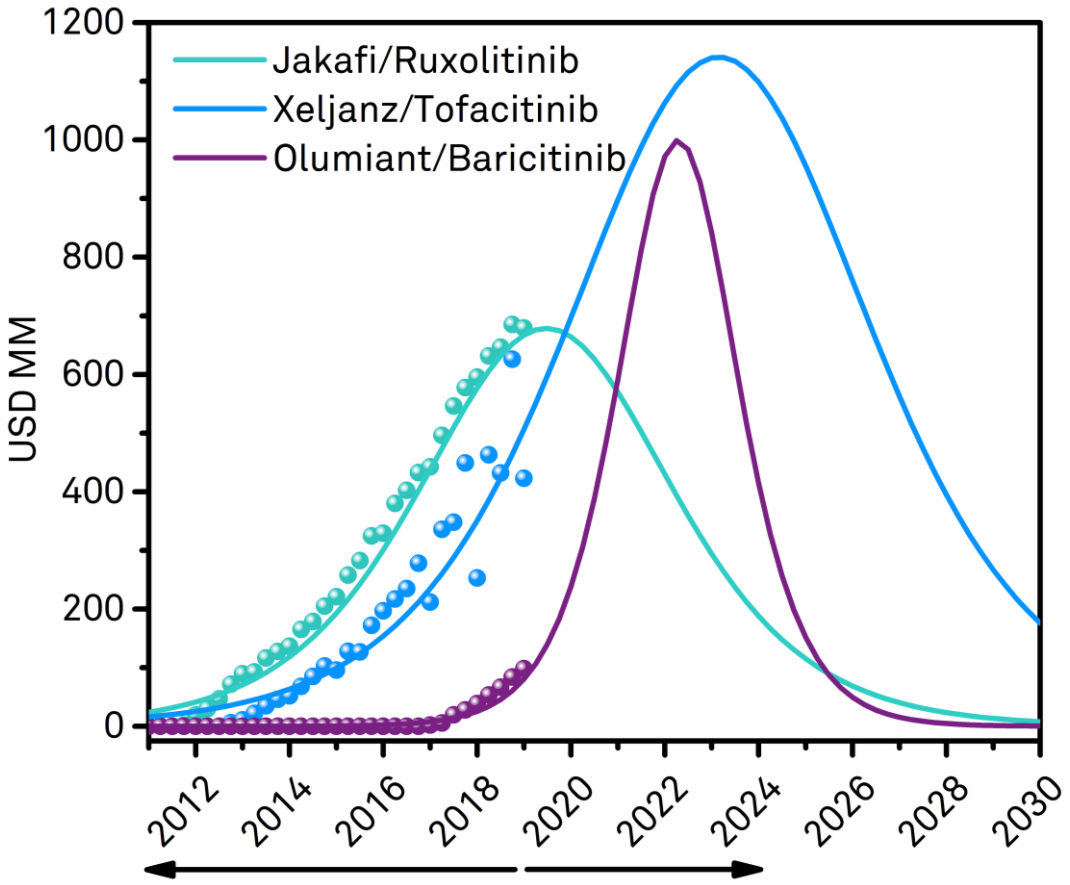
Equity analyst forecasts sourced from *Vantage*, EvaluatePharma

Bass Diffusion Model can predict future sales

How has the drug performed to date?

How is the drug doing compared to expectations?

How will the drug perform in the future?



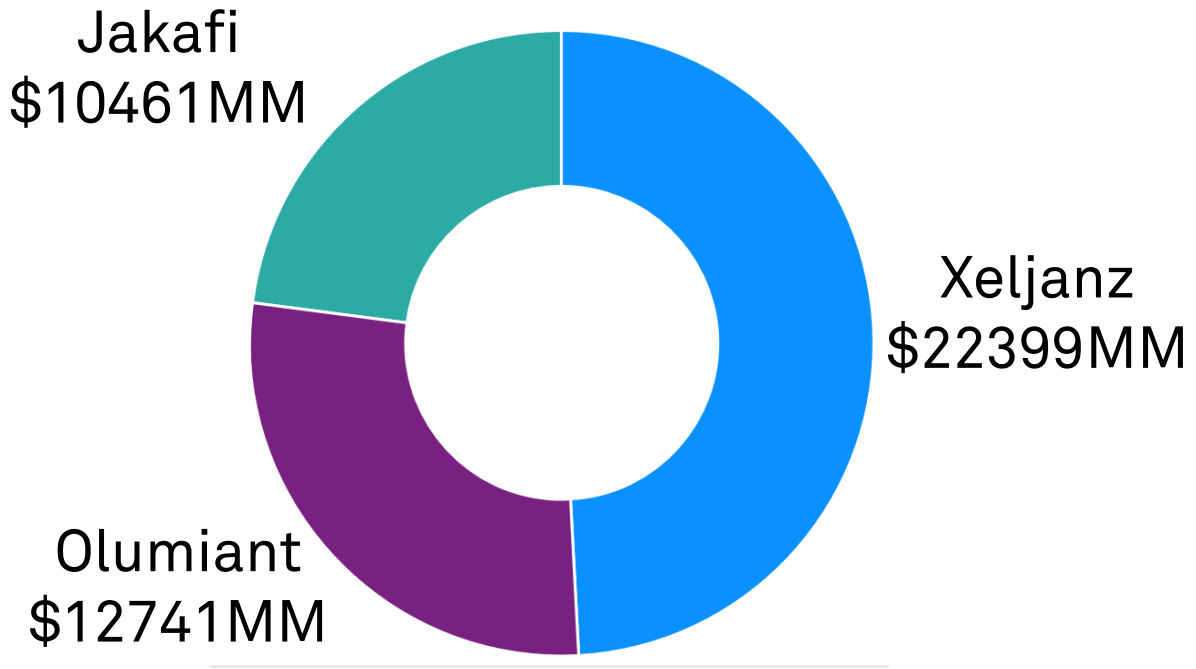


Chart 6. Reported quarterly sales for Jakafi, Xeljanz and Olumiant overlaid with sales figures predicted using the Bass model [left] and cumulative sales figures for the years 2019 – 2024 [right]

Drivers of peak sales for pharmaceutical brands, *Quantitative Marketing and Economics* 2010

Therapeutic Value of JAK inhibitors dictates Commercial Success

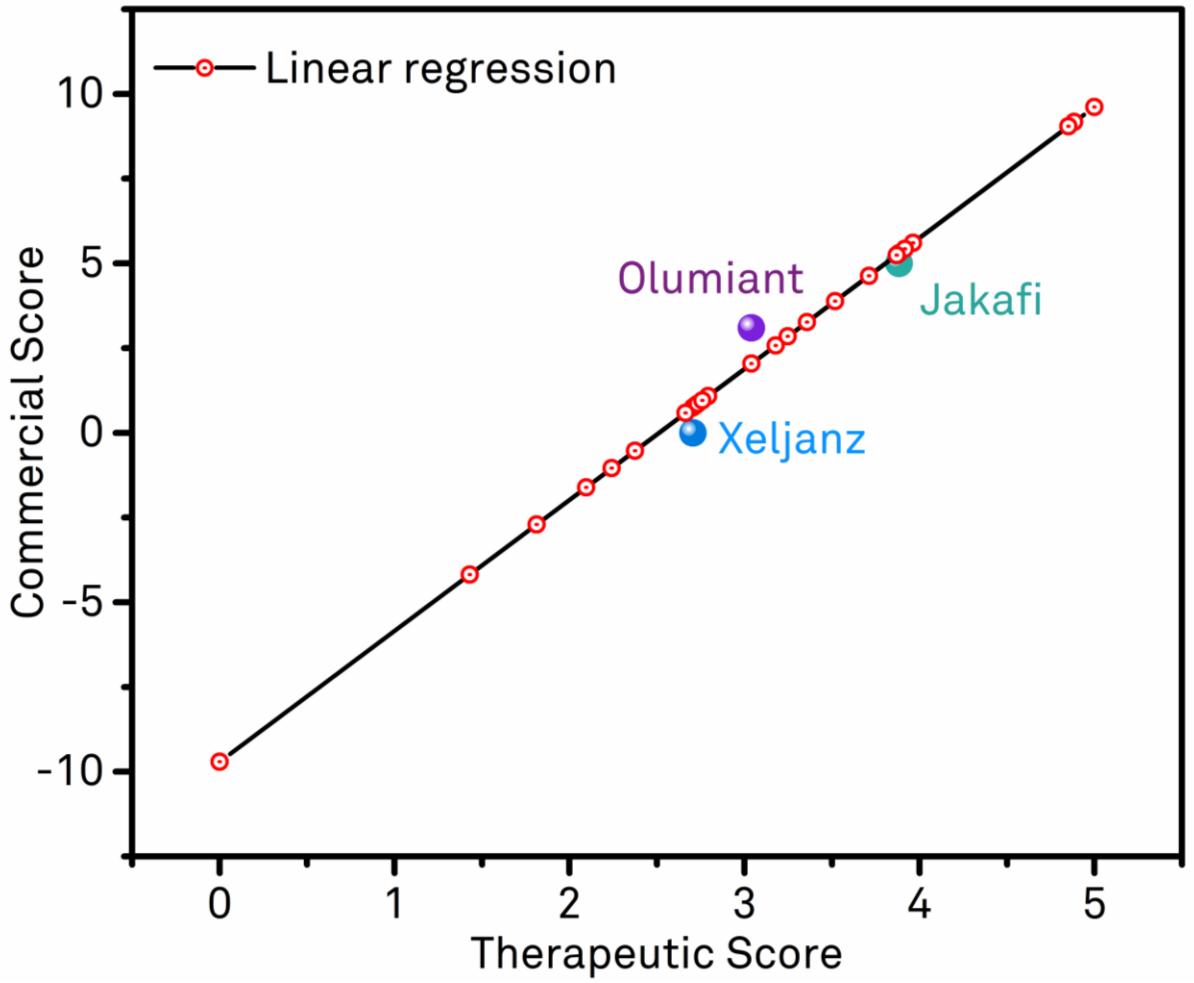


Chart 7. Therapeutic and commercial scores derived for JAK inhibitors

- Highest commercial scores: Pacritinib, BMS986165, Abrocitinib
- Multiple products with same mechanism tend to be approved in rapid succession – creating higher bar for differentiation
- Even in competitive market, better performance over standard of care translates to commercial success
- JAK inhibitors in the pipeline for multiple indications are more likely to be commercially durable

Trinity Drug Index **2016, 2017**, and **2018**; What drives success for specialty pharmaceuticals?, *Nature Reviews Drug Discovery* **2008**