

RACAPITAL

Global Differential Pricing

- Perspectives from Investors

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Key Questions

WHAT IS THE GLOBAL DRUG REVENUE THAT ACTUALLY INCENTIVIZES INNOVATION?

HOW IMPORTANT ARE US REVENUES FOR THE TOP 20 DRUGS IN INCENTIVIZING INNOVATION?

WHAT ARE THE LIKELY IMPACTS ON INNOVATION OF AN EFFECTIVE GLOBAL DIFFERENTIAL PRICING MECHANISM?

Let's start with the
\$1.5T of global
medicines spend at
invoice prices

Medicine spending and growth by product type varies by region

*at invoice prices!

	Original Brands	Non-Original brands	Unbranded Generics	Other	Total	
Spending 2022 US\$B	Global	902.1	244.5	150.2	185.5	1,482.3
	Developed	788.8	109.3	101.0	89.3	1,088.3
	10 developed	722.4	83.9	90.8	71.9	968.9
	Other developed	66.4	25.4	10.2	17.4	119.4
	Pharmerging	105.7	124.4	47.8	93.0	370.8
	Lower-income countries	7.7	10.8	1.5	3.2	23.2

Let's start with the \$1.5T of global medicines spend at invoice prices... of which ~\$600M is not original brands

Sales stemming from low-R&D work (e.g. generics, old reformulated medicine, and other non-original brands) do not incentivize investment in R&D-intensive work that leads to original brands (i.e. novel drugs). Society incentivizes that which it pays for. New medicines are incentivized by payments for new medicines. Payments for old medicines merely reward the making of old medicines.

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Innovators start with the \$900M of original brand spend, however, that is at invoice prices

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What is the branded drug revenue that actually incentivizes innovation?

We estimate **net spend WW of \$600-650B on original brands**

Includes ~200B in gross-to-net discounts in the US. Assuming most gross-to-net discounts are on the US market, we estimate \$600-650B of WW net spend on original brands

US medicine spend of \$629B at invoice price levels, of which 85.4% on original brands, for \$537B at invoice prices; IQVIA assumes 37% gtn for 'protected brands', for \$338B at net prices (~\$199B in gross-to net)

So, original brand "net" spend is more like \$600-700B

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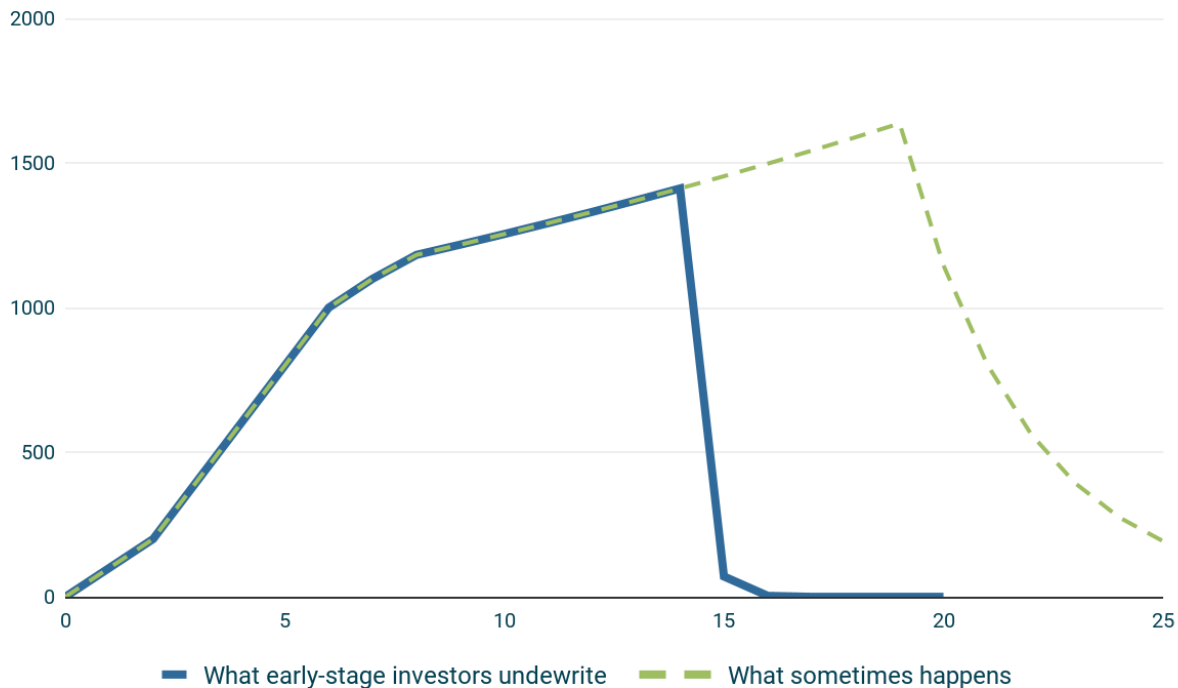
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And what incentivizes R&D investment are profits, not revenues, so keep in mind that margins are much lower on sales ex-US. The US is 5% of the global population and half the revenue for branded drugs. As complex as reimbursement in US is, it is a lot harder, takes longer, and is more expensive to ramp up sales across all the countries from which the other 50% of net revenues stem, so those profits are much lower, resulting in a low contribution to incentives for R&D investment.

And time matters...
 innovators do not view
 drug revenue that
 comprises \$600-650B
 on original brands
 equally...

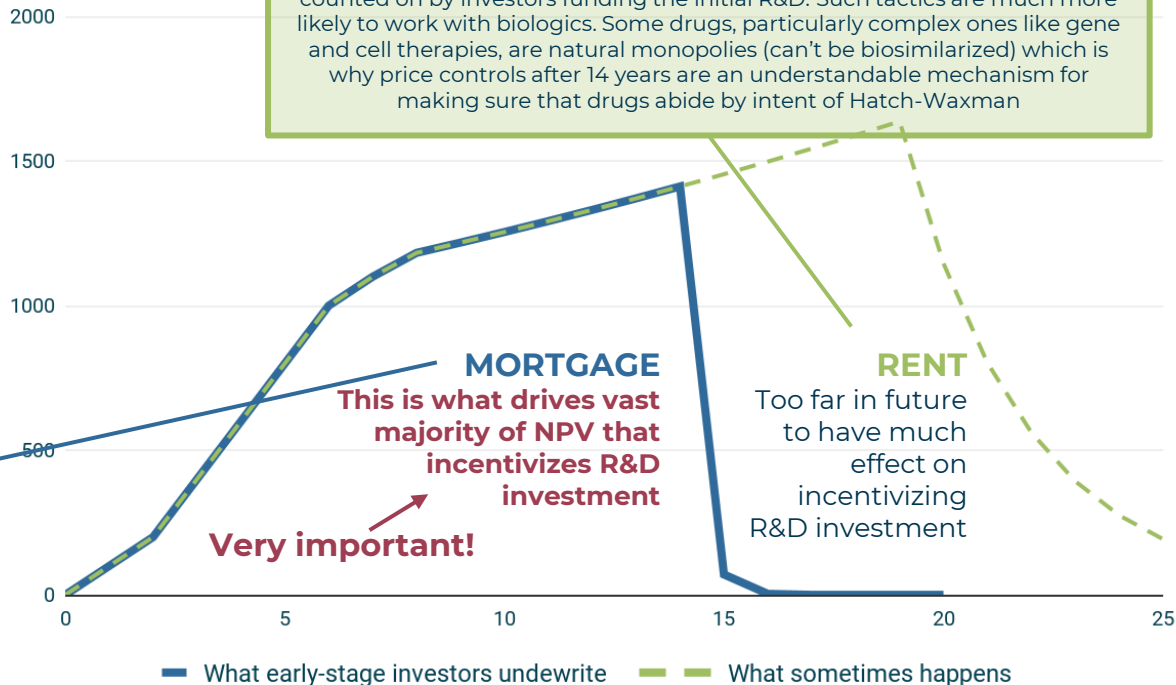
Sales



And time matters... innovators do not view drug revenue that comprises \$600-650B on original brands equally...

'Builders' underwrite to the 'mortgage' period granted by Hatch-Waxman, after which we assume the drug's price will be competed down by generic/biosimilar competition

Sales



Small companies still developing their first drugs are purely Builders focused on the Mortgage reward.

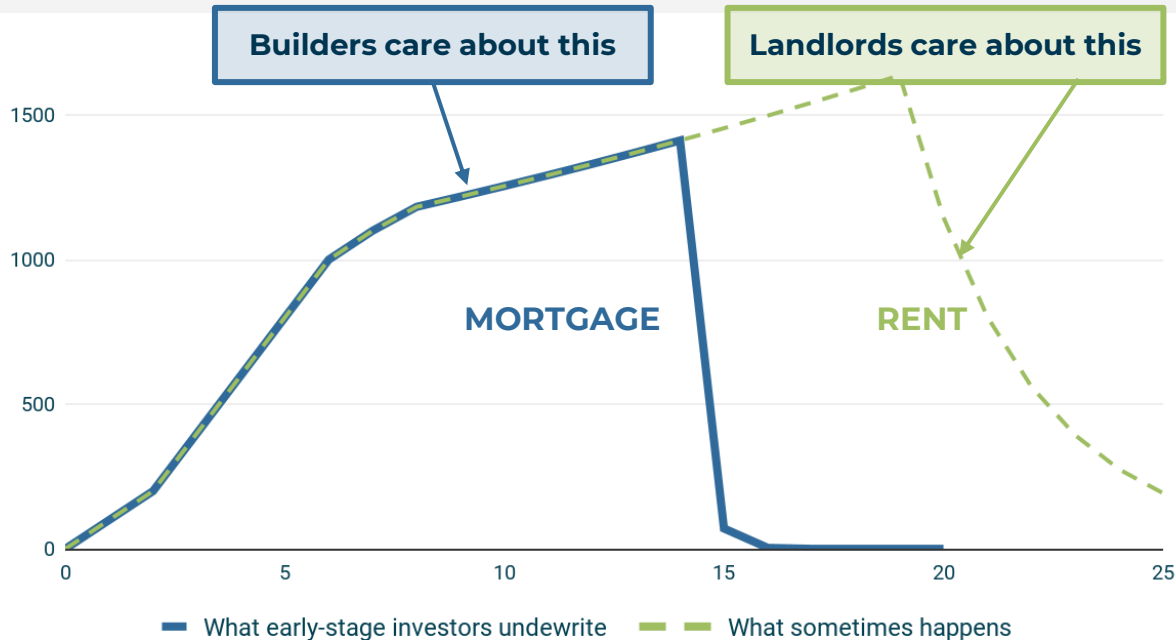
But industry has not historically spoken for Builders without being conflicted about giving up rent streams from aging products.

Some big biopharmas with both an R&D pipeline and mature profitable products (>14 years) are a hybrid of Builders and Landlords. Their internal Builders (e.g. heads of R&D) want to preserve the Mortgage streams. The Landlords can afford to see innovation extinguished as long as Rent streams are not entirely eliminated.

This is why some big biopharmas can seem to struggle to embrace “the biotech social contract” and can’t speak for small biotechs and their investors.

~2/3 of 2022 US revenue for drugs with reported sales were for drugs launched within 14 years.

Drug pricing reforms should **TARGET RENT** but **PRESERVE THE MORTGAGE.**



WHAT IS THE GLOBAL DRUG REVENUE THAT ACTUALLY INCENTIVIZES INNOVATION?

When we remove revenue for aged products, we estimate global revenue of \$400-430B for products in their Mortgage period

\$1.5T

Global medicines spend (ex-COVID) at invoice prices ^{*IQVIA}

⊖ ~\$600B

gx, non-original brands, other non-original ^{*IQVIA}

\$~900B

Original brand spend at invoice prices ^{*IQVIA}

⊖ ~\$200-350B

gross-to-net discounts ^{*IQVIA, RA Capital Estimates}

\$~600-650B

Original brand spend at net prices

⊖ ~\$200-220B

late-line products (older than 14 years) ^{*EvaluatePharma}

\$400-430B

Global revenue for innovative products

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Incentivizes ~\$200B of R&D spend/yr

(IQVIA R&D report: \$138B for top 15 pharmas in 2022, \$61B in venture capital and public biotech investments)

\$1.5T

Global medicines spend (ex-COVID) at invoice prices ^{*IQVIA}

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Global revenue for innovative products

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HOW IMPORTANT ARE US REVENUES FOR THE TOP 20 DRUGS IN INCENTIVIZING INNOVATION?

WHAT ARE THE LIKELY IMPACTS ON INNOVATION OF AN EFFECTIVE GLOBAL DIFFERENTIAL PRICING MECHANISM?

US revenues from the top 20 innovative drugs account for ~1/4 of total innovative drug revenue

2022 revenues for top-selling US drugs (ex-COVID, \$B)

Approved within 14 years of 2022

Rank by US sales	Drug	Company	Year Approved	Therapeutic Area	ALL DRUGS ex COVID		INNOVATIVE DRUGS
					US revenue		US revenue
1	Humira	AbbVie Inc	2002	Immunology	18,619		
2	Keytruda	Merck & Co Inc	2014	Oncology	12,686		12,686
3	Biktarvy	Gilead Sciences Inc	2018	Infectious Disease	8,510		8,510
4	Revlimid	Bristol-Myers Squibb Co	2005	Oncology	8,359		
5	Eliquis	Bristol-Myers Squibb Co	2012	Cardiovascular	7,786		7,786
6	Dupixent	Sanofi	2017	Dermatology	6,673		6,673
7	Stelara	Johnson & Johnson	2009	Immunology	6,388		6,388
8	Eylea	Regeneron Pharmaceuticals Inc	2011	Ophthalmology	6,265		6,265
9	Trulicity	Eli Lilly and Co	2014	Metabolic Disorders	5,689		5,689
10	Ozempic	Novo Nordisk AS	2017	Metabolic Disorders	5,478		5,478
11	Opdivo	Bristol-Myers Squibb Co	2014	Oncology	4,812		4,812
12	Ocrevus	F. Hoffmann-La Roche Ltd	2017	Central Nervous System	4,701		4,701
13	Skyrizi	AbbVie Inc	2019	Immunology	4,484		4,484
14	Darzalex/Faspro	Johnson & Johnson	2015	Oncology	4,189		4,189
15	Enbrel	Amgen Inc	1998	Immunology	4,044		
16	Prevnar 13/Prevenar 13	Pfizer Inc	2010	Infectious Disease	4,032		4,032
17	Entyvio	Takeda Pharmaceutical Co Ltd	2014	Gastrointestinal	3,634		3,634
18	Imbruvica	AbbVie Inc	2013	Oncology	3,426		3,426
19	Ibrance	Pfizer Inc	2015	Oncology	3,370		3,370
20	Gammagard	Takeda Pharmaceutical Co Ltd	1986	Immunology	2,889		
21	Cosentyx	Novartis AG	2015	Immunology	2,770		2,770
22	Vyvanse	Takeda Pharmaceutical Co Ltd	2007	Central Nervous System	2,750		
23	Invega Sustenna/Xeplion/Trinza /Trevicta	Johnson & Johnson	2009	Central Nervous System	2,714		2,714
24	Orencia	Bristol-Myers Squibb Co	2005	Immunology	2,638		
25	Xtandi	Astellas Pharma Inc	2012	Oncology	2,525		2,525
26	Xarelto	Johnson & Johnson	2011	Cardiovascular	2,473		2,473
TOTAL:					141,904		102,605

Out of \$400-430B Global Innovation Drug Spend

CBO PRESENTATION 11.8.2023

GLOBAL revenues from the top 20 innovative drugs in the US account for ~1/3 of total innovative drug revenue

Approved within 14 years of 2022

2022 revenues for top-selling US drugs (ex-COVID, \$B)

Rank by US sales	Drug	Company	Year Approved	Therapeutic Area	ALL DRUGS (ex COVID)		INNOVATIVE DRUGS	
					US revenue	Global revenue	US revenue	Global revenue
1	Humira	AbbVie Inc	2002	Immunology	18,619	21,237		
2	Keytruda	Merck & Co Inc	2014	Oncology	12,686	20,937	12,686	20,937
3	Biktarvy	Gilead Sciences Inc	2018	Infectious Disease	8,510	10,390	8,510	10,390
4	Revlimid	Bristol-Myers Squibb Co	2005	Oncology	8,359	9,978		
5	Eliquis	Bristol-Myers Squibb Co	2012	Cardiovascular	7,786	11,789	7,786	11,789
6	Dupixent	Sanofi	2017	Dermatology	6,673	8,720	6,673	8,720
7	Stelara	Johnson & Johnson	2009	Immunology	6,388	9,723	6,388	9,723
8	Eylea	Regeneron Pharmaceuticals Inc	2011	Ophthalmology	6,265	6,265	6,265	6,265
9	Trulicity	Eli Lilly and Co	2014	Metabolic Disorders	5,689	7,440	5,689	7,440
10	Ozempic	Novo Nordisk AS	2017	Metabolic Disorders	5,478	8,446	5,478	8,446
11	Opdivo	Bristol-Myers Squibb Co	2014	Oncology	4,812	8,249	4,812	8,249
12	Ocrevus	F. Hoffmann-La Roche Ltd	2017	Central Nervous System	4,701	6,323	4,701	6,323
13	Skyrizi	AbbVie Inc	2019	Immunology	4,484	5,165	4,484	5,165
14	Darzalex/Faspro	Johnson & Johnson	2015	Oncology	4,189	7,946	4,189	7,946
15	Enbrel	Amgen Inc	1998	Immunology	4,044	4,117		
16	Prevnar 13/Prevenar 13	Pfizer Inc	2010	Infectious Disease	4,032	6,337	4,032	6,337
17	Entyvio	Takeda Pharmaceutical Co Ltd	2014	Gastrointestinal	3,634	5,191	3,634	5,191
18	Imbruvica	AbbVie Inc	2013	Oncology	3,426	2,394	3,426	2,394
19	Ibrance	Pfizer Inc	2015	Oncology	3,370	5,120	3,370	5,120
20	Gammagard	Takeda Pharmaceutical Co Ltd	1986	Immunology	2,889	3,858		
21	Cosentyx	Novartis AG	2015	Immunology	2,770	4,788	2,770	4,788
22	Vyvanse	Takeda Pharmaceutical Co Ltd	2007	Central Nervous System	2,750	3,393		
23	Invega Sustenna/Xeplion/Trinza /Trevicta	Johnson & Johnson	2009	Central Nervous System	2,714	4,140	2,714	4,140
24	Orencia	Bristol-Myers Squibb Co	2005	Immunology	2,638	3,464		
25	Xtandi	Astellas Pharma Inc	2012	Oncology	2,525	4,884	2,525	4,884
26	Xarelto	Johnson & Johnson	2011	Cardiovascular	2,473	2,473	2,473	2,473
TOTAL:					141,904	192,767	102,663	146,720

Out of \$400-430B Global Innovation Drug Spend

HOW IMPORTANT ARE US REVENUES FOR THE TOP 20 DRUGS IN INCENTIVIZING INNOVATION?

We estimate the top 20 drugs account for >50% of industry profit from marketed products (*before considering R&D for indication expansion or new products*)

	WW		The Rest
	TOTAL	TOP 20	
Revenue	\$430B	\$147B	\$283B
COGS	20%	10%	25%
SG&A	25%	8%	34%
Maintenance R&D	5%	1%	7%
Contribution margin	50%	81%	34%
EBIT from marketed products	\$215B	\$119B	\$96B
%TOTAL:		55%	45%
COGS	\$86B	\$15B	\$71B
SG&A	\$108B	\$12B	\$96B
Maintenance R&D	\$22B	\$1B	\$20B

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Impact of a Global Differential Pricing Model That Enables Everyone to Pay Their “Fair” Share

- Earlier access for ex-US patients
- Broader access for ex-US patients
- Greater incentives for innovation, including in disease states that have higher prevalence ex-US, due to:
 - Higher ex-US profits
 - More certainty in ex-US pricing and timing