

Traditional Drug Trend

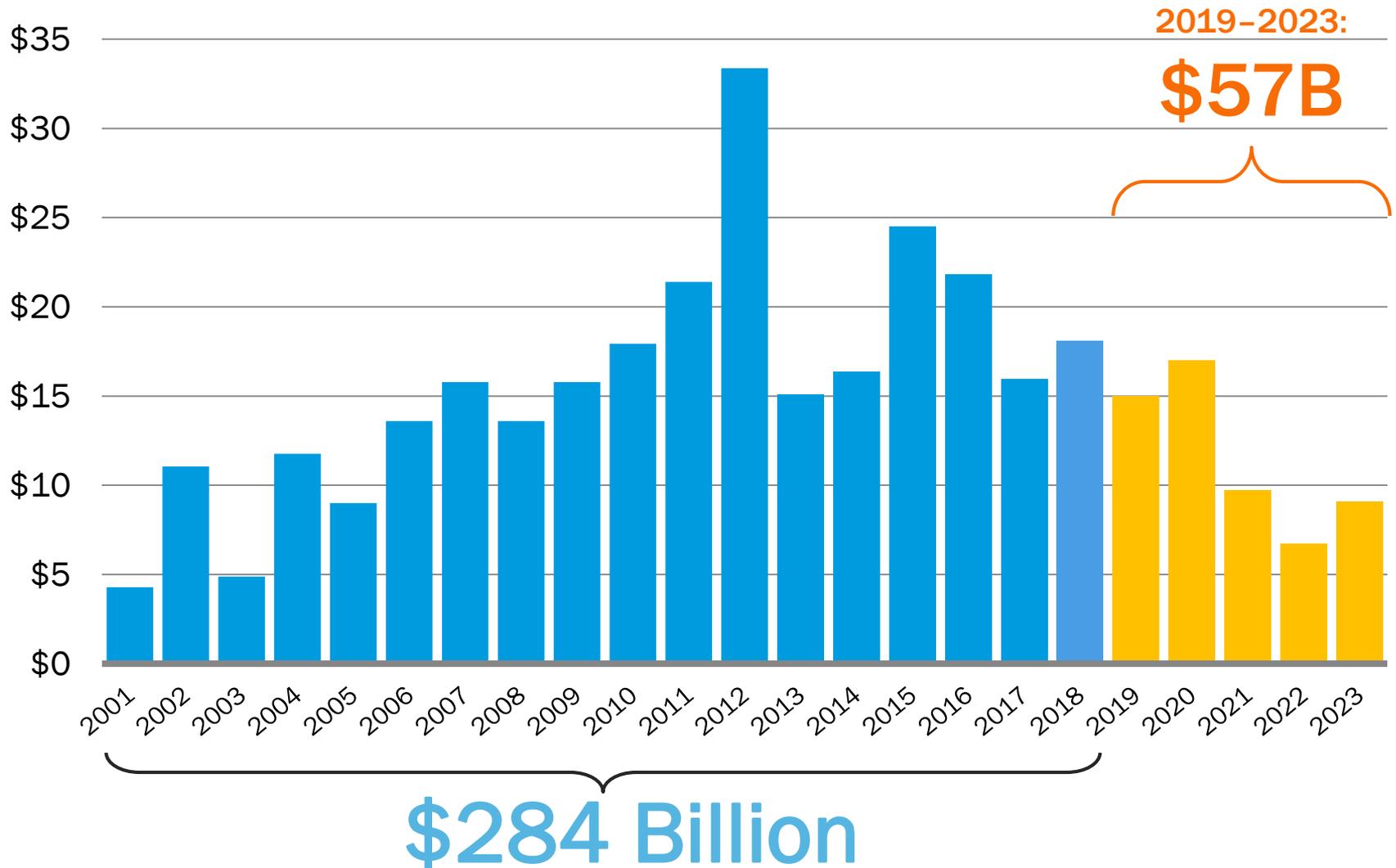


2018 Landscape in Review

Topic	
FDA Approvals	<p>In 2018, the FDA has approved a record number of novel drugs, known as new molecular entities (NME's) and biologic license applications (BLA's). FDA has approved 59 novel products, 36 of which are considered specialty and 23 traditional medications.</p>
FDA New Drug Approvals	<p>Some of the more notable TRADITIONAL drug approvals include:</p> <ul style="list-style-type: none"> • Aemcolo™ (rifamycin SV MMX) • AndexXa® (andexanet alfa) • Aimovig™ (erenumab-aooe) • Ajovy™ (fremanezumab-vfrm) • Emgality™ (galcanezumab-gnlm) • Jornay PM™ (methylphenidate) • Oxervate (cenegermin) • Orilissa™ (elagolix) • Motegrity™ (prucalopride) • Xofluza™ (baloxavir marboxil)
First-Time Generics	<p>In 2018, \$11.2 billion in first time generics have launched. Some of the larger selling generics include:</p> <ul style="list-style-type: none"> • Aloxi® Injection • Adcirca® • Androgel 1.62% • Cialis® • EpiPen® • Levitra® • Makena® • Namenda XR® • Norvir® Tablets • Onfi® • Prevacid SoluTab™ • Sustiva® 600mg Tabs • Welchol® • Zytiga® 250mg



Patent Expiration Landscape



2018 New Generic Approvals

Brand Name	Primary Indication	Annual Sales (millions)	Date Generic Launched
Adcirca	Pulmonary Hypertension	\$483	Aug. 13
Brevibloc Premixed	High Blood Pressure/Heart Disease	\$73	Sep. 06
Ampyra	Multiple Sclerosis	\$248	Sep. 13
Sporanox oral solution	Fungal Infections	\$14	Sep. 19
Albenza tablets	Parasitic Infections	\$99	Sep. 24
Cialis	Erectile Dysfunction	\$1,932	Sep. 27
Evekeo	ADHD	\$50	Sep. 28
Trisenox	acute promyelocytic leukemia	\$67	Oct. 03
Androgel 1.62%	Hormonal Supplementation	\$1,048	Oct. 15
Onfi	Seizures	\$594	Oct. 23
Levitra	Erectile Dysfunction	\$127	Oct. 31
Finacea gel	Acne	\$64	Nov. 20
EpiPen Auto-Injector	Anaphylaxis	\$763	Nov. 27
Zytiga	Prostate Cancer	\$1,373	Dec. 03
Canasa	inflammatory Conditions	\$244	Dec. 17



2018 New Generic Approvals

Brand Name	Primary Indication	Annual Sales (millions)	Date Generic Launched
Istodax	Cancer	\$48	Jan. 11
Ultiva	Pain and Inflammation	\$71	Jan. 17
Sustiva 600mg Tablets	HIV	\$113	Feb. 01
Syprine	Chelation Therapy	\$155	Feb. 09
Treximet (85/500)	Migraine	\$102	Feb. 15
Namenda XR	Alzheimer's Disease	\$936	Feb. 20
Solodyn 65mg and 115mg	Acne	\$148	Feb. 20
Prevacid Solutab	Heartburn/Ulcer Disease	\$184	Mar. 08
Norvir Tablets	HIV	\$296	Mar. 12
Safyral	Contraceptives	\$24	Mar. 13
Topicort 0.25% Topical Spray	Skin Conditions	\$19	Mar. 19
Aloxi Injection	Nausea/Vomiting	\$459	Mar. 23
Zavesca	Enzyme Deficiencies	\$107	Apr. 23
Welchol	High Blood Cholesterol	\$526	May. 17
Invanz	Infections	\$375	Jun. 28
Makena	Hormonal Supplementation	\$231	Jul. 02
Uceris tablets	inflammatory Conditions	\$197	Jul. 09
Cosopt PF	Glaucoma	\$17	Jul. 30
Adcirca	Pulmonary Hypertension	\$483	Aug. 13
Torisel	Cancer	\$35	Aug. 13



Key Brand Drugs Losing Patent Protection

About \$70 billion within the next five years

2019	2020	2021	2022	2023
(Annual Sales)				
\$16.3 Billion	\$17 Billion	\$9.7 Billion	\$6.7 Billion	\$9.1 Billion
<ul style="list-style-type: none"> • Afinitor • Emend Inj. • Exjade • Faslodex • Lyrica • Ranexa • Solodyn (55mg, 80mg, & 105mg) • Tarceva • Tekturna • Vesicare 	<ul style="list-style-type: none"> • Absorica • Chantix • CiproDex • Daliresp • Dexilant • Latuda • Noxafil • Silenor • Tecfidera • Tykerb • Uloric • Velcade • Viibryd 	<ul style="list-style-type: none"> • Amitiza • Atripla • Brovana • Bystolic • Intelence • Northera • Performist • Pradaxa • Suprep bowel prep kit • Sutent • Truvada 	<ul style="list-style-type: none"> • Abraxane • Afinitor • Alimta • Banzel • Combigan • Prezista • Suboxone SL film • Rayos • Treanda • Velcade • Vimpat 	<ul style="list-style-type: none"> • Aggrastat • Duexis • Janumet • Januvia • Kombiglyze XR • Livalo • Onglyza • Riomet • Trokendi XR • Tyzeka • Votrient • Xyrem



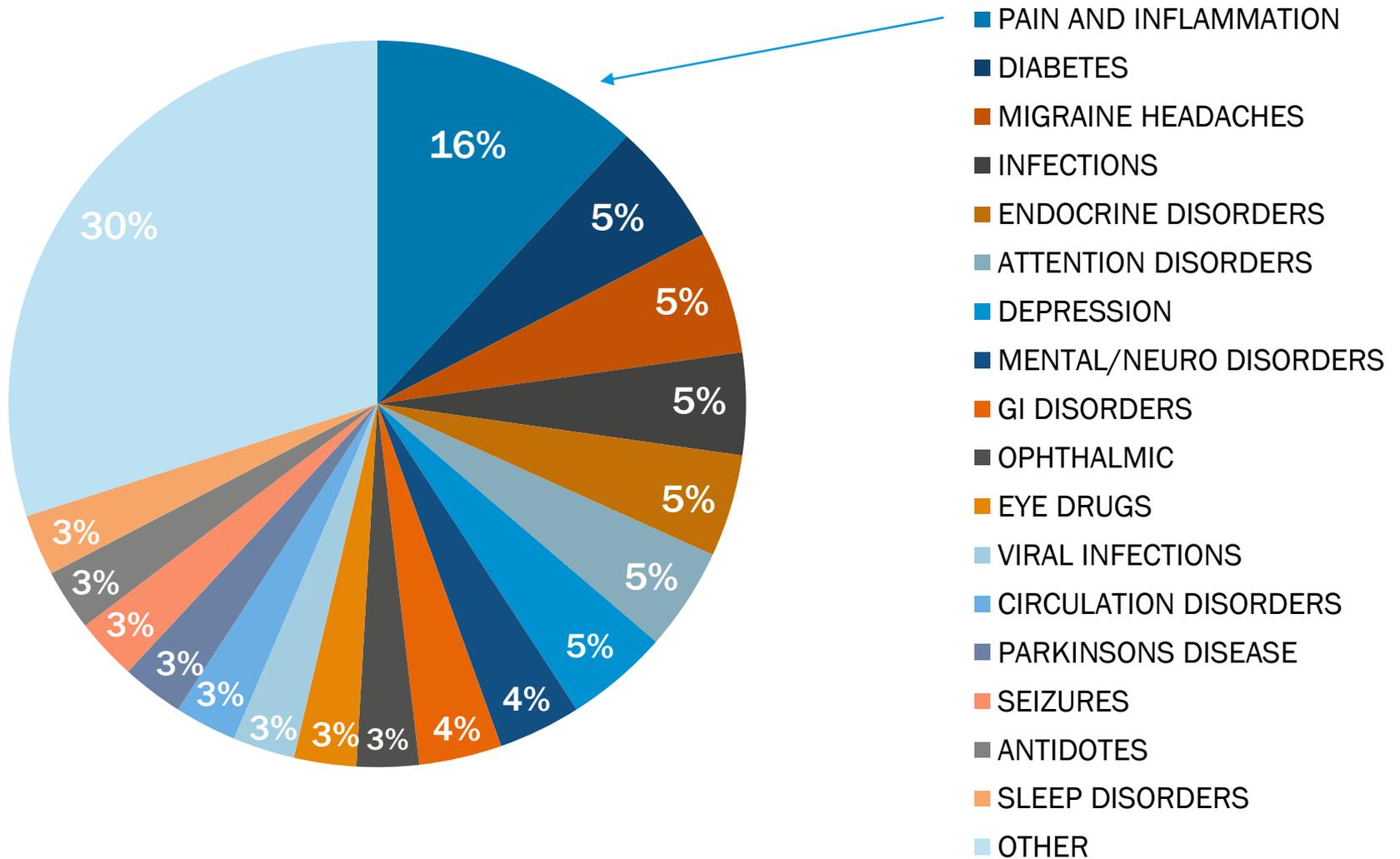
Blockbuster Generics? Looking Forward

Generic	
Advair Diskus	Mylan's AB-rated generic to Advair Diskus is currently under FDA review. Approval could occur any day. Other manufactures developing generics to Advair Diskus include Sandoz (2019), Hikma/Vectura (2020). Advair had \$4.3 billion in annual sales in 2017.
Restasis	The main patents on Restasis, blocking generics from launching, were invalidated in Oct. 2017. These patents are also undergoing review by the US Patent Office. While this review, along with the appeal of the patent ruling are ongoing, generics could launch "at risk". However, FDA has yet to approve an A-rated generic. Approval could occur at any time.
ProAir HFA	Due to a patent settlement agreements, Perrigo and Lupin can launch upon FDA approval. However, complex device and drug product make final approval challenging. Approval could occur in 2019 or 2020 followed by a launch shortly after.



Traditional drug pipeline

Proportion of near-term traditional pipeline drugs by indication



Near-Term Traditional Pipeline Highlights

Drug	Indication
apomorphine sublingual film	Parkinson's Disease
fexapotide triflutate	Benign Prostatic Hyperplasia
Inbrija (levodopa, inhaled)	Parkinson's Disease
lasimiditan	Migraine
lumateperone	Schizophrenia

Drug	Indication
MyGluca (glucagon rescue pen)	Hypoglycemia
Pearl Triple (budesonide/formoterol/glycopyrronium)	COPD
Semglee (insulin glargine)	Diabetes
Viaskin Peanut	Peanut Hypersensitivity
Zynquista (sotagliflozin)	Diabetes, Type 1



Select Traditional Pipeline Drug Details

Drug	Manufacturer	Indication	Mechanism	Comments
fexapotide triflutate	Nymox	Benign Prostatic Hyperplasia	pro-apoptotic protein	An antineoplastic treatment for benign prostatic hyperplasia. The drug acts through neural thread proteins which kills cells treating benign tumors, including BPH; intraprostatic injection.
lasimiditan	Lilly/CoLucid	Migraine	Serotonin 1F receptor agonists	Also known as "ditans", for the acute treatment of migraine headaches. Lasimiditan has similar efficacy to, but without the vasoconstrictor side effects associated with triptan. Oral therapy.
Viaskin Peanut	DBV Technologies	Peanut Allergies	Peanut immunotherapy	Transdermal system (patch) that delivers small amounts of peanut protein to help desensitize patients to this protein to help avoid potentially life-threatening allergic reactions in children 4-11 years old; transdermal patch.
Zynquista (sotagliflozin)	Lexicon/Sanofi	Type 1 diabetes	dual SGLT1 and SGLT2 inhibitor	Sotagliflozin is an oral, first-in-class, dual inhibitor of sodium glucose transporters 1 and 2 (SGLT1 & 2) for use, in combination with insulin therapy, to improve glycemic control in adults with type 1 diabetes mellitus.

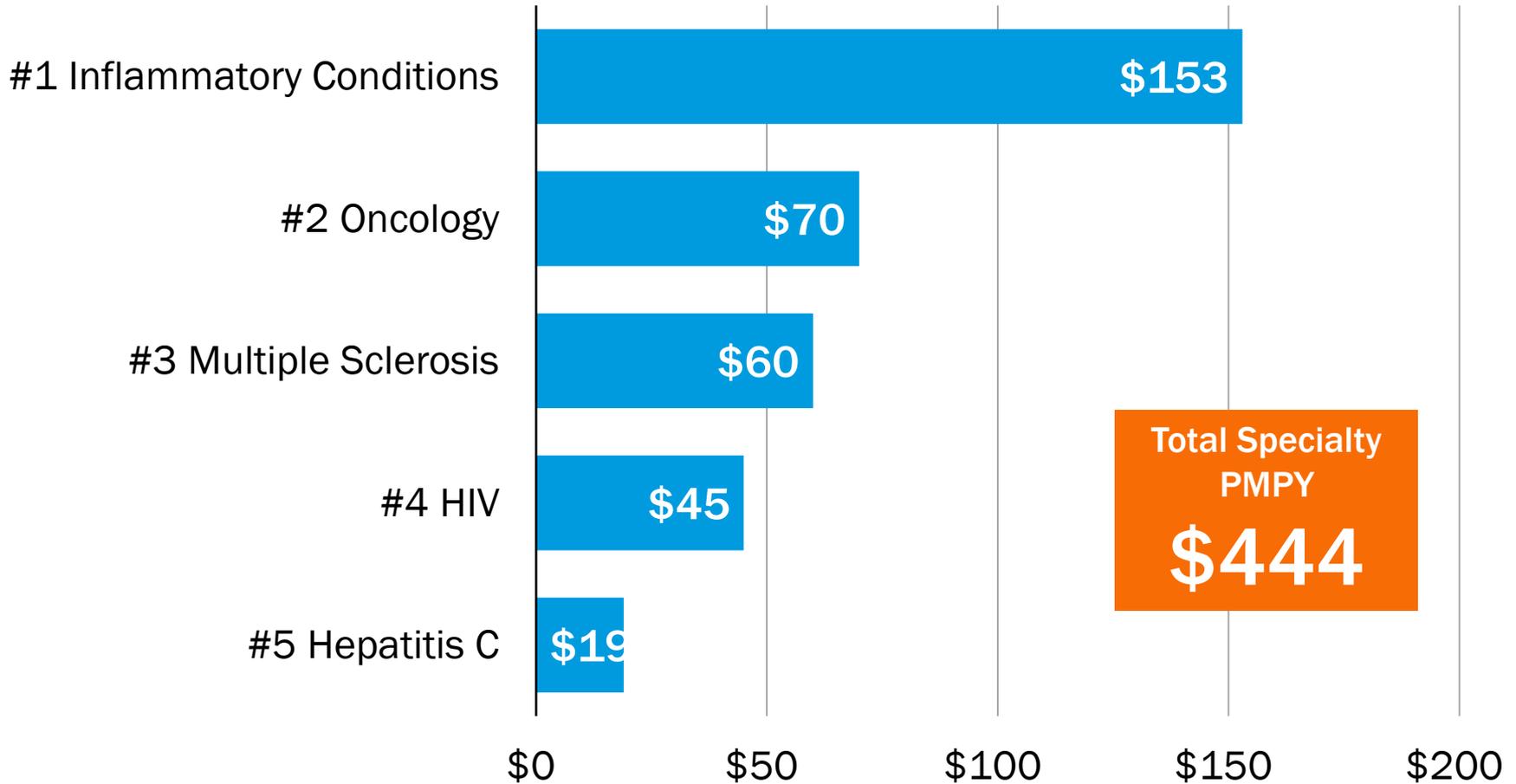
Specialty Drug Trend



Leading specialty therapy classes

Pharmacy-adjudicated claims only

2017 PMPY



Source: Express Scripts' 2017 Drug Trend Report



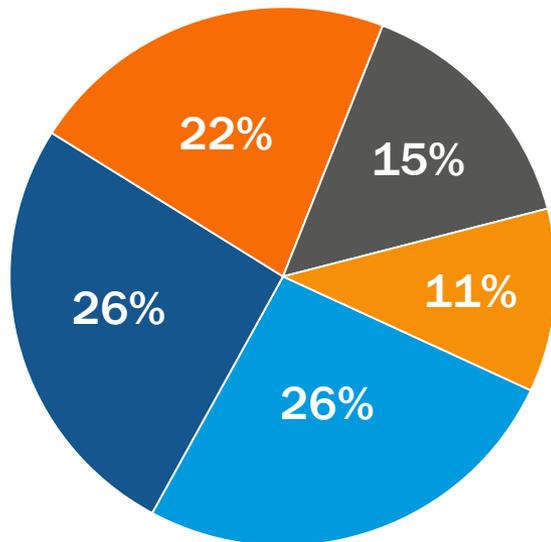
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Specialty drug pipeline

Proportion of near-term specialty pipeline drugs by indication

- Cancer
- Orphan Conditions
- Biosimilars
- Other
- Multiple Sclerosis



Significant specialty medications approved during 2017

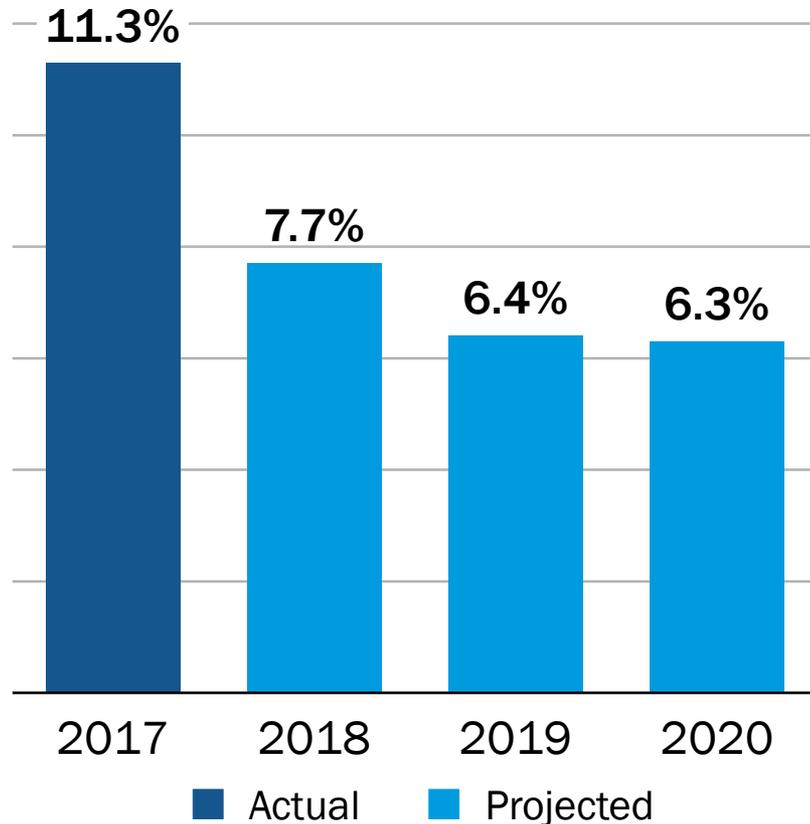
Drug	Indication*	Annual cost (est.)
Bavencio	MCC	\$156,000
Dupixent	Atopic dermatitis	\$37,000
Ocrevus	Multiple sclerosis	\$65,000
Austedo	HD chorea	\$60,000
Ingrezza	Tardive dyskinesia	\$64,000
Imfinzi	Bladder cancer	\$148,000
Tremfya	Psoriasis	\$58,000
Idhifa	AML	\$300,000
Kymriah	ALL	\$475,000

*MCC = Merkel Cell Carcinoma; HD = Huntington's Disease; AML = Acute Myeloid Leukemia; ALL = Acute Lymphoblastic Leukemia

Projected specialty trend

PBM-adjudicated claims only

Total specialty trend



Select therapy classes	2018	2019	2020
Inflammatory conditions*	16.0%	15.0%	14.0%
Oncology*	17.0%	13%	11.3%
Multiple sclerosis	-4.2%	-7.9%	-4.0%
HIV	11.5%	11.1%	10.4%
Hepatitis C	-11.1%	-0.1%	-1.6%

*forecasting data includes specialty and traditional drugs in this therapy class



Near-term specialty pipeline highlights

Drug	Indication	Drug	Indication
brolocizumab	Age-related macular degeneration	lisocabtagene maraleucel	Lymphoma (NHL*)
celiprolol	Vascular Ehlers-Danlos syndrome	onasemnogene abeparvovec	Spinal muscular atrophy
cladribine	Multiple sclerosis	ozanimod	Multiple sclerosis
diroximel fumarate	Multiple sclerosis	quizartinib	Leukemia (AML*)
entinostat	Breast cancer	ravulizumab	Paroxysmal nocturnal hemoglobinuria
erdafitinib	Urothelial cancer	risankizumab	Psoriasis
fenfluramine	Dravet syndrome	romosozumab	Osteoporosis
givosiran	Acute intermittent porphyria	tafamidis	Amyloidosis
golodirsen	Duchenne muscular dystrophy	upadacitinib	Rheumatoid arthritis

Bold = Details on the following slide

*NHL = Non-Hodgkin Lymphoma; AML = Acute Myeloid Leukemia



Select specialty pipeline drug details

Drug	Manufacturer	Indication	Mechanism	Comments
erdafitinib	Janssen	FGFR+ advanced or metastatic urothelial cancer	Pan-fibroblast growth factor receptor (FGFR) inhibitor; Oral therapy	Erdafitinib is an oral (once-daily) FGFR inhibitor for the treatment of FGFR+ advanced or metastatic urothelial cancer. Approval expected by May 18, 2019.
lisocabtagene maraleucel	Celgene	Diffuse large B-cell lymphoma (DLBCL)	Chimeric antigen receptor T (CAR-T) cell therapy; IV infusion	Lisocabtagene maraleucel is a CAR-T cell therapy administered as a one-time IV infusion for the second-line treatment of relapsed or refractory DLBCL. Approval is expected in early-2019.
onasemnogene abeparvovec	Novartis	Spinal muscular atrophy (SMA) Type 1	Survival motor neuron 1 gene therapy; IV infusion	Onasemnogene abeparvovec is a gene therapy administered as a one-time IV infusion to treat infants with SMA Type 1. Approval is expected in early-2019.
risankizumab	AbbVie / Boehringer Ingelheim	Plaque psoriasis	Interleukin-23 inhibitor; SC therapy	Risankizumab is an interleukin-23 inhibitor administered every 12 weeks by SC injection for the treatment of moderate-to-severe plaque psoriasis. Approval is expected by Apr. 25, 2019.



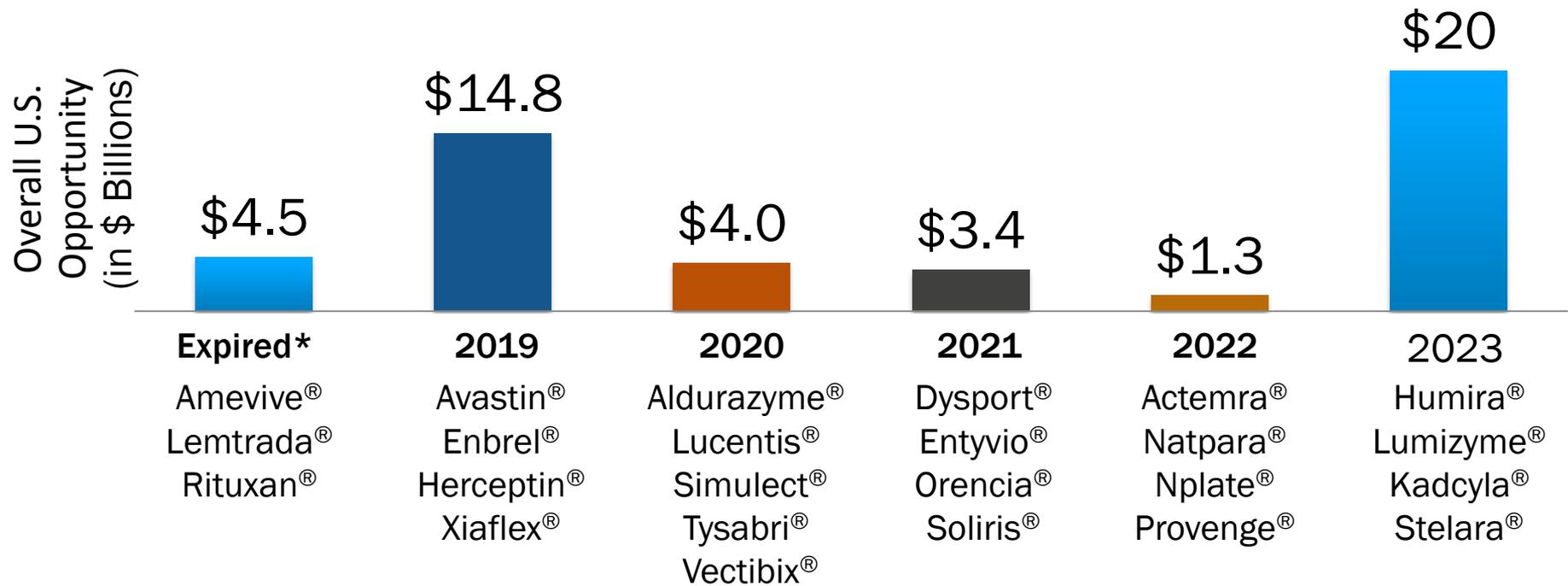
Biosimilar Drug Trend



Biosimilar Future Opportunity

\$55B OPPORTUNITY

71 PATENT EXPIRATIONS THROUGH 2023



*Includes biologic drugs that have had key patents expire. Source: U.S. Drug spend estimates are based on IQVIA data for 2017. The patent expiration dates of the biologic products is current as of March 2018. Patent expiration does not necessarily imply biosimilar availability. The availability of biosimilars is highly variable due to litigation, patent challenges, FDA's establishment of 351(k) pathway, or other factors. Trademarks are the property of their respective owners, brand names being used in this slide for illustrative purposes.



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Challenges to projecting biosimilar availability

Projected FDA approval dates do not have to be publically disclosed

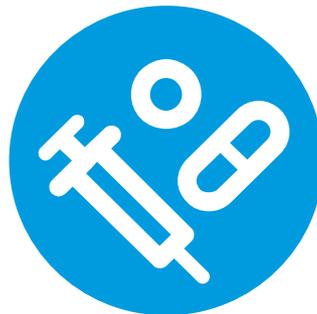
- Some manufacturers announce FDA action dates while others do not

FDA approval does not mean the biosimilar has launched

- The launch of a biosimilar product is ultimately a business decision

Patent expiration does not imply biosimilar availability

- Innovator companies hold multiple patents for each biologic medication
- Patent litigation is expected to delay biosimilar launch in many cases
- Biosimilar companies have to prove they don't infringe on non-expired patents
- If a biosimilar manufacturer launches "at-risk", or before patent litigation is resolved, they may be subject to significant financial penalties if the patents are ultimately ruled valid and infringed



Settlement agreements could alter projected launch dates

- Terms within these agreements are typically not publically disclosed

Approved biosimilar products

Biosimilar	Innovator	Approval	Launch
Zarxio (filgrastim-sndz) Manufacturer: Sandoz	Neupogen (Amgen)	Mar. 6, 2015	Sep. 3, 2015
Inflectra (infliximab-dyyb) Manufacturer: Pfizer/Celltrion	Remicade (Janssen)	Apr. 5, 2016	Nov. 28, 2016
Erelzi (etanercept-szzs) Manufacturer: Sandoz	Enbrel (Amgen)	Aug. 30, 2016	TBD (litigation ongoing)
Amjevita (adalimumab-atto) Manufacturer: Amgen	Humira (AbbVie)	Sep. 23, 2016	Jan. 31, 2023 (settlement agreement)
Renflexis (infliximab-abda) Manufacturer: Merck/Samsung	Remicade (Janssen)	Apr. 21, 2017	July 24, 2017
Cylteza (adalimumab-adbm) Manufacturer: Boehringer Ingelheim	Humira (AbbVie)	Aug. 25, 2017	TBD (litigation ongoing)



Approved biosimilar products (continued)

Biosimilar	Innovator	Approval	Launch
Mvasi (bevacizumab-awwb) Manufacturer: Amgen/Allergan	Avastin (Genentech)	Sept. 14, 2017	TBD (litigation ongoing)
Ogivri (trastuzumab-dkst) Manufacturer: Mylan/Biocon	Herceptin (Genentech)	Dec. 1, 2017	TBD (litigation ongoing)
Ixifi (infliximab-dyyb) Manufacturer: Pfizer	Remicade (Janssen)	Dec. 13, 2017	No Plans to Commercialize
Retacrit (epoetin alfa-epbx) Manufacturer: Hospira	Epogen (Amgen) Procrit (Janssen)	May 15, 2018	June 13, 2018
Fulphila (pegfilgrastim-jmdb) Manufacturer: Mylan/Biocon	Neulasta (Amgen)	June 4, 2018	July 30, 2018
Nivestym (pegfilgrastim-aafi) Manufacturer: Pfizer	Neulasta (Amgen)	July 20, 2018	Oct. 1, 2018



Approved biosimilar products (continued)

Biosimilar	Innovator	Approval	Launch
Hyrimoz (adalimumab-adaz) Manufacturer: Sandoz	Humira (AbbVie)	Oct. 31, 2018	Sep. 30, 2023 (settlement agreement)
Udenyca (pegfilgrastim-cbqv) Manufacturer: Coherus	Neulasta (Amgen)	Nov. 2, 2018	Jan. 2019
Herzuma (trastuzumab-pkrb) Manufacturer: Celltrion/Teva	Herceptin (Genentech)	Dec. 14, 2018	TBD (litigation ongoing)



Biosimilar Strategy – 2019 and beyond

First-time biosimilars expected to launch in 2019

- Avastin
- Enbrel
- Herceptin
- Rituxan

Obstacles to shifting marketplace

- Sensitivity to changing medication
- Existing copay assistance programs
- HUB involvement
- New formulations developed

Strategy

- Brand for generic differential (BGDiff)
- 3-Tier benefit design for specialty medications
 - Generic
 - Brand (Preferred)
 - Brand (Non-Preferred)

