2021 FDA Drug Approvals – What You Need to Know

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Program Objectives

At the completion of this activity, pharmacists will be able to*:*

1. Identify new medications approved to fill a need with orphan diseases
2. Discuss the place in therapy for new drugs with novel mechanisms of action
3. Describe what is meant by a “breakthrough drug” and provide an example of one approved in 2021

At the completion of this activity, pharmacy technicians will be able to*:*

1. Identify an orphan drug approved by the FDA in 2021
2. Match five new medications and their indications
3. Provide an example of a medication considered to be a breakthrough drug

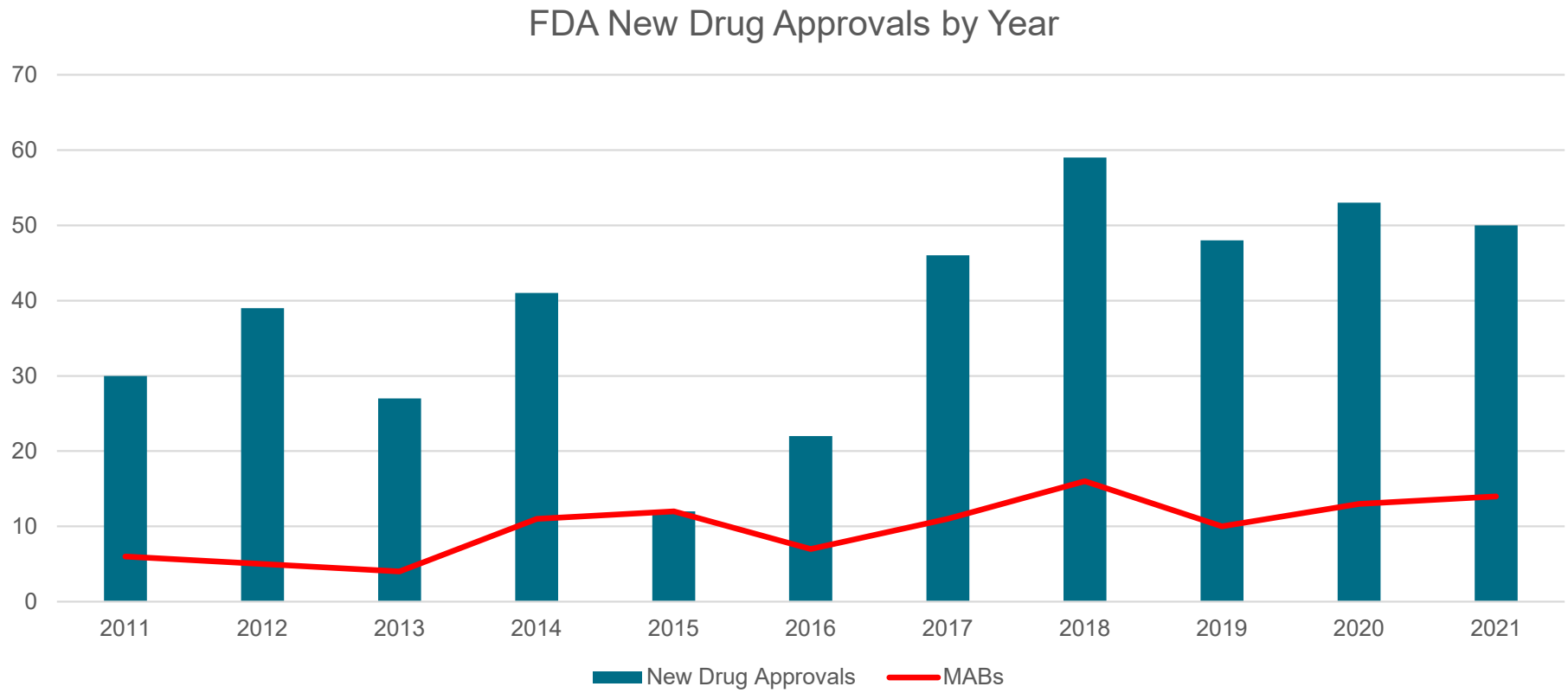
Disclosures

I have no disclosures to report

I will be using both generic and brand names of medications and may discuss both FDA-approved and non-FDA-approved indications

Warning: I may be mispronouncing generic and trade drug names

History of FDA Drug Approvals



In 2021, 50 NMEs approved, 14 MABs

2021 FDA Drug Approvals

- Adbry (tralokinumab-ldrm)
- Aduhelm (aducanumab-avwa)
- Amondys 45 (casimersen)
- Azstarys (serdexmethylphenidate; dexmethylpher
- Besremi (ropeg 2b-njft)
- Brexafemme (ib
- Bylvay (odevixil
- Cabenuva (cabo rilpivirine)
- Cosela (trilacicl
- Cytalux (pafola
- Empaveli (pegcetacoplan)
- Evkeeza (evinacumab-dgnb)
- Exkivity (mobocerinib)
- Fexinidazole (fexinidazole)
- Fotivda (tivozanib)
- Jemperli (dostarlimab-gxly)
- Kerendia (finerenone)
- Korsuva (difelikefalin)
- Leqvio (inclisiran)
- Livmarli (maralixibat)
- Livtencity (maribavir)
- Lumakras (sotorasib)

How many of the new drugs of 2021 are you familiar with?

- flufenamide)
- Ponvory (ponesimod)
- Pylarify (piflufolastat F 18)
- Qelbree (viloxazine)
- Qulipta (atogepant)
- Rezurock (belumosudil)
- Rybrevant (amivantamab-vmjw)
- Rylaze (asparaginase erwinia chrysanthemi(recombinant)-rywn)
- Saphnelo (anifrolumab-fnia)
- Scemblix (asciminib)
- somatropin-tcgd)
- avacopan)
- (tepotinib)
- tezepelumab-ekko)
- sotumab vedotin-
- (infigratinib)
- mbralisib)
- Verquvo (vericiguat)
- Voxzogo (vosoitide)
- Vyvgart (efgartigimod alfa-fcab)
- Welireg (belzutifan)
- Zegalogue (dasiglucagon)
- Zynlonta (loncastuximab tesirine-lpyl)

Audience Poll #1

Which one of the following statements is true?

A. Orphan drug designation is given for a drug that is indicated for a disease that afflicts at least 1 million people in the U.S.

B. Trials based on surrogate endpoints are not permitted as the basis for approval of first-in-class drugs

C. FDA can suggest a product be submitted as a breakthrough drug

D. Fast track status and priority review are the same thing

Special Review Designation Types

Designation	Definition	Provisions	# in 2021
Orphan drug	Product to prevent, diagnose or treat a rare disease or condition • 200,000 or fewer patients in the U.S • Request submitted by sponsor	• Tax credits for qualified clinical trials • Exemption from user fees • Potential 7 years of market exclusivity	26
First-in-class	Novel mechanism of action	Surrogate endpoints can be used for drugs fulfilling unmet needs	27
Breakthrough Status	Process for expedited development and review when preliminary evidence demonstrates substantial improvement in at least one clinically significant endpoint over available therapies • Requested by drug company • FDA may suggest drug company consider submitting a request • Request ideally received by FDA by end of phase 2	Eligible for expedited review, fast track status Allows for FDA guidance on efficient drug development, as early as Phase 1	14

Special Review Designation Types

Designation	Definition	Provisions	# in 2021
Standard Review	Usual process for approval of new drugs	FDA takes action on the new drug application within 10 months	13
Priority Review	For drugs that significantly improve the treatment, diagnosis and prevention of serious conditions	FDA takes action of the new drug application within 6 months	34
Fast Track Review	Process for facilitated development and review of drugs that treat serious conditions, fill unmet needs and have promising animal or human data • Requested by drug company at any time during drug development	Eligible for: • Frequent meetings and communications with FDA to discuss drug development and collection of data to support approval • Eligible for accelerated and priority approval • Rolling review of BLA or NDA	18
Accelerated Approval	For promising therapies of serious or life-threatening conditions that fill an unmet medical need • Useful when disease course is long and an extended period of time is needed to measure its effect on the disease	Can use a surrogate endpoint for approval or a clinical endpoint that occurs earlier but may not be as robust as a standard endpoint • Confirmatory post-marketing clinical trials needed	14

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New Drugs of 2021

New Drug Approvals 2021 – Anti-Infectives

New Anti-Infective Agents

- **Brexafemme (ibrexafungerp)**
  - Oral triterpenoid antifungal (**first-in-class**) for treatment of vulvovaginal candidiasis
    - 300 mg twice daily for one day; available as 150 mg tablets
    - Inhibits the enzyme glucan synthase – important in fungal cell wall formation
    - Joins fluconazole as an oral option to treat this condition
    - Being studied for refractory fungal infections; IV formulation in development
- **Fexinidazole (fexinidazole)**
  - Oral nitroimidazole for treatment of first- and second-stage human African trypanosomiasis (aka Sleeping Sickness) for patients 6 years and older; ≥ 20 kg
    - First all-oral treatment developed under Drugs for Neglected Diseases initiative
    - Once daily for 10 days (4 days loading dose; 6 days maintenance dose)
  - Orphan drug manufactured in partnership with National Sleeping Sickness Programs of the Democratic Rep of Congo and Central African Republic and Sanofi

Brexafemme [package insert]. Jersey City, NJ: Scynexis, Inc. 2021

Fexinidazole [package insert]. Bridgewater, NJ; Sanofi-Aventis, U.S. LLC. 2021

New Drug Approvals 2021 – Anti-Infectives

New Anti-infective Agents

- **Livtencity (maribavir)** – **first-in-class**, orphan, breakthrough medication
  - Treatment of post-transplant CMV infection refractory to treatment with ganciclovir, valganciclovir, cidofovir or foscarnet
    - Unique MOA: inhibits CMV's pUL97 protein kinase, inhibiting phosphorylation and CMV virus replication
    - 400 mg twice daily (200 mg tablets)
    - Drug interactions
      - CYP3A4 substrate, weak CYP3A4 inhibitor
      - Avoid co-administration with ganciclovir and valganciclovir (maribavir reduces their efficacy)
  - Resistance – mutation developed in 2 of 119 patients in Phase 2 trial
  - Higher rate of GI adverse drug events compared to valgancicllovir in trials; higher rate of discontinuation of treatment

Livtencity [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S., Inc. 2021

N Engl J Med 2019;381:1136-47. DOI: 10.1056/NEJMoa1714656

New Drug Approvals 2021 – Anti-Infectives

- Other medications for CMV infections
  - Prevymis (letermovir)
    - approved in **2017** for prophylaxis of CMV with allogeneic hematopoietic stem cell transplant; once daily PO/IV; also has a unique MOA
  - Leflunamide and artesunate
    - not approved for CMV infection but have been used alone or in combination for resistant infections
  - Brincidofovir
    - long half-life and twice weekly dosing
    - **investigational medication** with clinical trials underway (mixed results)
    - Prodrug to cidofovir

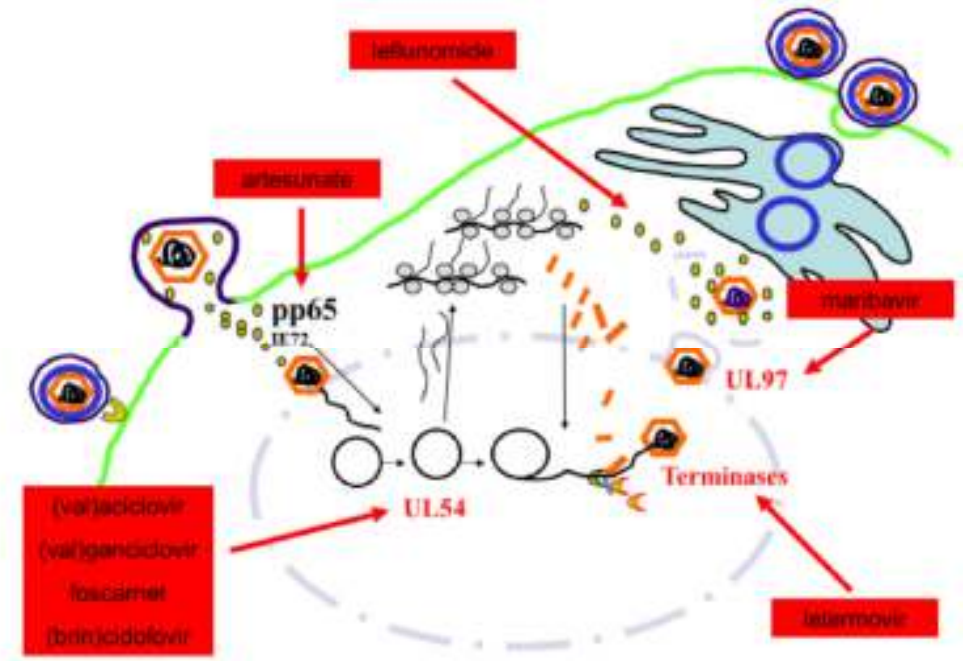


Fig. 1. Flow chart of CMV life cycle and targets of available antivirals or antivirals in development.

https://doi.org/10.1016/j.medmal.2018.03.006

New Drug Approvals 2021 – Blood, Mineral & Electrolyte Disorders

New Cholesterol Lowering Medications

Evkeeza (evinacumab-dgnb)

- **First-in-class**, orphan drug, breakthrough medication
  - Indication: homozygous familial hypercholesterolemia (HoFH) in patients ≥ 12 years old
    - As adjunct to other LDL-C lowering therapies
  - MOA: angiopoietin-like 3 (ANGPTL3) inhibitor
    - ANGPTL-3 inhibits lipoprotein lipase activity leading to increased triglycerides and other lipids
  - Dosing: 15 mg/kg by IV infusion over 60 minutes once monthly
  - Elipse Phase 3 trial: reduces LDL-C by 47% at week 24

Evkeeza [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc. 2021

Leqvio (inclisiran)

- **First-in-class** medication
  - MOA: small interfering RNA (siRNA) directed to PCSK9 mRNA
    - inhibits PCSK9 by a different mechanism than other PCSK9 inhibitors
  - Indication – heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease in adults who require additional lowering of LDL-C
  - Adjunct to maximally tolerated statin therapy
  - Dosing: 284 mg subcutaneously x1, second injection at 3 months, followed by every 6 months
  - Orion Phase 3 clinical trials: reduces LDL-C by 50% at 18 months

Leqvio[package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp, 2021

New Drug Approvals 2021 – Blood, Mineral & Electrolyte Disorders

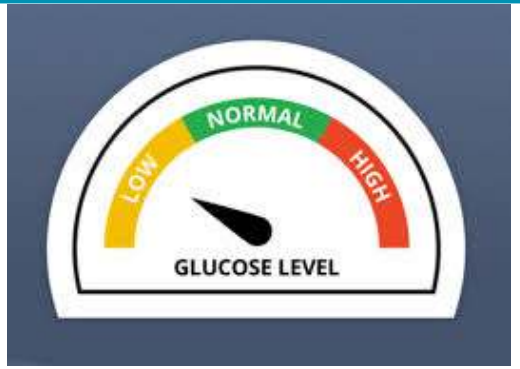
Homozygous vs Heterozygous Familial Hypercholesterolemia

Type	Prevalence	Symptoms	Risks	Treatments
Heterozygous familial hypercholesterol-emia (HeFH)	1 in every 200-300 people worldwide - Common genetic disorder	LDL-C ≥ 190 mg/dL in adults; ≥ 160 mg/dL in children	CAD in 40's or 50's	Statins, bile-acid sequestrants, exetimide, fibrates, nicotinic acid, PCSK9 inhibitors
Homozygous familial hypercholesterol-emia (HoFH)	1 in every million people worldwide - Rare genetic disorder	LDL-C > 400 mg/dL; tendon xanthomas and coronary heart disease occur in childhood	CAD and aortic stenosis often seen in teenage years; untreated patients rarely live past age 30	Same as above plus aggressive treatment including LDL apheresis

CAD = coronary artery disease

https://rarediseases.org/rare-diseases/familial-hypercholesterolemia/

New Drug Approvals 2021 – Blood, Mineral & Electrolyte Disorders

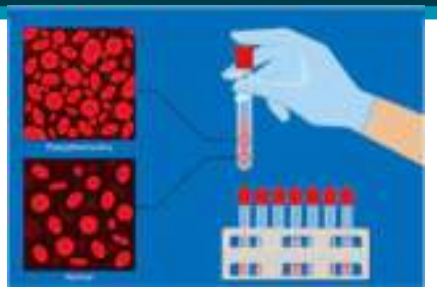


Zegalogue (dasiglucagon)

- Glucagon receptor agonist to treat severe hypoglycemia episodes in patients ≥ 6 years with diabetes
  - Activates hepatic glucagon receptors – stimulates glycogen breakdown – release of glucagon from the liver
  - Rescue treatment instructions:
    - Administer 0.6 mg SQ with autoinjector and pre-filled syringe
    - Call for emergency assistance
    - If no response after 15 minutes, can administer a second dose (from second kit)
    - When patient responds to treatment, give oral carbohydrates

Zegalogue [package insert]. Soborg, Denmark: Zealand Pharma A/S. 2021

New Drug Approvals 2021 – Blood, Mineral & Electrolyte Disorders



Besremi (ropeginterferon alfa-2b-njft)

- **First-in-class** interferon alfa-2b
- Orphan drug for treatment of adults with polycythemia vera
  - Overproduction of RBCs and increased incidence of blood clots and stroke
- Dosing:
  - 100-500 mcg SQ every 2 weeks (start with 50 mcg if transitioning from hydroxyurea)
  - Can reduce dosing interval to every 4 weeks after 1 year of treatment
- Boxed Warnings: fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders
- PEGINVERA – Phase I/II trial with 51 patients over 7.5 years; 31 patients had complete hematologic response for median duration of 14.3 months
- Contraindications: psychiatric disorders, hypersensitivity to interferons, mod-sev hepatic disease, automimmune disease, immunosuppressed transplant patients

Besremi [package insert]. Burlington, MA: PharmaEssentia USA Corporation. 2021
Blood (2018) 132 (Supplement 1): 3030. https://doi.org/10.1182/blood-2018-99-118584

New Drug Approvals 2021 – Blood, Mineral & Electrolyte Disorders

Empaveli (pegcetacoplan)

- Orphan drug for paroxysmal nocturnal hemoglobinuria (PNH) in adults
  - Main concerns of patients with PNH = anemia, fatigue, need for transfusions
- MOA: **first-in-class** pegylated pentadecapeptide inhibiting complement (C3) which controls both intravascular and extravascular hemolysis
- Boxed warning for serious infections with encapsulated bacteria (e.g., *Strep pneumoniae, Neisseria meningitidis, and Haemophilus influenzae*)
  - **REMS program** to assure patients are vaccinated at least 2 weeks prior to receiving first dose
- Dosing: 1080mg SQ infusion twice weekly (via commercially available pump)
- PEGASUS Phase 3 clinical trial – 48-week trial comparing pegcetacoplan vs eculizumab (C5 inhibitor) in PNH patients with hemoglobin < 10.5/dL while on eculizumab for ≥ 3 months
  - 16 weeks randomized controlled portion followed by 32-week open-label with pegcetocoplan
  - Pegcetocoplan superior to eculizumab at 16 weeks based on change in hemoglobin level from baseline

Empaveli [package insert]. Waltham, MA: Apellis Pharmaceuticals. 2021

N Engl J Med 2021;384:1028-37. DOI: 10.1056/NEJMoa2029073

New Drug Approvals 2021 – Cardiovascular Disorders

Verquvo (vericiguat)

- **First-in-class**, fast track and priority review
- Indication: symptomatic chronic heart failure and ejection fraction < 45% (HFrEF)
  - Reduces risk of CV death and hospitalization following a hospitalization for heart failure or need for outpatient IV diuretics
- MOA: soluble guanylate cyclase (sGC) stimulator – improves levels of cyclic GMP leading to smooth muscle relaxation and vasodilation
- Dosing: 2.5 mg orally once daily; double dose every 2 weeks to 10 mg once daily
  - Boxed Warnings: causes fetal harm
- VICTORIA Phase 3 trial – 5050 patients followed over a median of 10.8 months; vericiguat added to current treatment
  - Primary outcome: composite of death from CV causes or first hospitalization for heart failure; 35.5% vericiguat group vs 38.5% placebo group (P=0.02); 10% relative risk reduction

Verquvo [package insert]. Whitehouse Station, NJ: Merck & Co, Inc. 2021
N Engl J Med 2020; 382:1883-1893 DOI: 10.1056/NEJMoa1915928

New Drug Approvals 2021 – Endocrine and Metabolic Diseases

Nulibry (fosdenopterin)

- **First-in-class**, orphan, breakthrough and priority review; rare pediatric disease designation
- Indication: **Molybdenum Cofactor Deficiency (MoCD) Type A** (confirmed by genetic testing)
  - an ultra-rare, life-threatening, genetic, metabolic disorder in newborns (150 patients world-wide); leading to intractable seizures, brain injury and death
- MOA: replaces cyclic pyranopterin monophosphate (cPMP) allowing molybdenum cofactor synthesis steps to proceed as normal and prevent disease complications
- Daily IV infusion of 0.4-0.9 mg/kg (1.5 mL/min) – dose based on age and prematurity
- Adverse Effects: photosensitivity; catheter-related complications (89%), pyrexia (78%); viral infection (56%), pneumonia, otitis media, vomiting, coughing/sneezing
- Clinical trials – 13 patients from 2 prospective, open-label, single-arm, dose-escalation trials and one retrospective, observational trial comparing patients in a natural history study
  - Survival probability at 1 and 3 years – 92% and 84% in treated group vs 67% and 55% in untreated group; risk of death 82% lower in treated group

Nulibry [package insert]. Boston, MA: Origin Biosciences, Inc. 2021

New Drug Approvals 2021 – Endocrine and Metabolic Diseases

Skytrofa (lonapegsomatropin-tcgd)

- Orphan Drug Indication: growth failure due to inadequate secretion of endogenous growth hormone in pre-pubertal children ≥ 1year old and ≥ 11.5 kg
  - for treatment-naïve patients or previously on daily somatropin treatment
- MOA: pegylated human growth hormone (GH); binds to GH receptor in cell membrane with direct tissue and metabolic effects
  - Prodrug with "transient conjugation" that allows slow release of active drug
- Dosing: 0.24 mg/kg SQ once weekly
- Clinical trials – Phase 3 heiGHt trial in 161 treatment-naïve patients; found both non-inferior and superior to somatropin in 52-week growth velocity
- Other new growth hormone agents:
  - Somapacitan-beco (Sogroya®) - weekly, growth hormone analog approved in 2020 for adult GH deficiency
  - Somatrogon – weekly recombinant human growth hormone for pediatric patients awaiting FDA approval

Skytrofa [package insert]. Hellerup, Denmark: Ascendis Pharma Endocrinology Division A/S. 2021

New Drug Approvals 2021 – Immune Diseases

Tavneos (avacopan)

- **First-in-class**, orphan drug for severe vasculitis (ANCA-associated) as an adjunct to standard therapy including glucocorticoids
  - ANCA (anti-neutrophil cytoplasmic antibody) is an autoantibody that targets and attacks neutrophils
  - ANCA-associated vasculitis is an autoimmune disease with destruction and inflammation of small blood vessels affecting kidneys, stomach, intestines, and lungs; skin lesions (purpura and urticaria) occur when blood vessels swell/bleed under the skin
- MOA: complement 5a receptor (C5aR) antagonist
  - Blocks C5a-mediated neutrophil activation and migration
- Dosing: 3 x 10 mg capsules orally twice daily with food
  - DI with CYP3A4 inhibitors - reduce dose to 30mg once daily with concomitant use
- Warnings: hepatotoxicity; angioedema; hepatitis B reactivation; serious infections
- ADVOCATE Phase 3 trial – R/DB, active-controlled (prednisone) - non-inferior to prednisone at week 26; superiority in sustained remission at week 52
- Provides a new era of targeted therapy for ANCA-associated vasculitis

Tavneos [package insert]. Cincinnati, OH: Thermo Fisher Scientific for ChemoCentryx Inc. 2021

New Drug Approvals 2021 – Immune Diseases

Saphnelo (anifrolumab-fnia)

- Indication: Systemic lupus erythematosus (SLE)
  - adult patients with moderate to severe SLE, receiving standard therapy
- MOA: **first-in-class**, receptor antagonist blocking activity of type 1 interferons
  - Reduces inflammation and immunologic response
- Dosing: 300mg via 30-minute IV infusion every 4 weeks
- Clinical trials
  - TULIP-1 trial failed to show statistical signif at 52 weeks with primary endpoint (improvement in SLE-responder index-4 versus placebo), although secondary endpoints favored anifrolumab
  - TULIP-2 trial demonstrated statistical signif with the previous trial's secondary endpoint as its primary endpoint
    - composite end points – 1) disease activity response; 2) reduction in glucocorticoid dose, and 3) reduction in severity of skin disease
  - Place in therapy – add on to other standard treatments; may allow for reduction in oral corticosteroid dose

Saphnelo [package insert]. Wilmington, DE: AstraZeneca. 2021

New Drug Approvals 2021 – Kidney Diseases

Lupkynis (voclosporin)

- Indication: adults with active lupus nephritis
  – addition to regimen of mycophenolate mofetil and corticosteroids
- MOA: **first-in-class**, new generation calcineurin-inhibitor, immunosuppressant
- Boxed Warning: increased risk for severe infections and malignancies
  - Can cause nephrotoxicity, hypertension, neurotoxicity, hyperkalemia, QT prolongation
- Dosing: starting dose 23.7mg orally once daily

eGFR: only use if eGFR > 45 mL/min/1.73m^2
- Adjust dose if eGFR drops below 60 mL/min/1.73m2
- Monitor eGFR q2weeks in first month, then monthly

BP: not recommended if BP > 165/105 mmHg
- Monitor BP q2weeks in first month, then prn

Discontinue if no benefit after 24 weeks

- Metabolized by CYP3A4 and drug interactions with strong or moderate CYP3A inhibitors and potent or moderate inducers
- AURORA Phase 3 clinical trial – complete renal response at week 52 in 41% of voclosporin patients vs 23% of patients with placebo ($p<0.0001$)

Lupkynis [package insert]. Rockville, MD: Aurinia Pharma. 2021
Lancet 2021; 397: 2070–80. https://doi.org/10.1016/ S0140-6736(21)00578-X

New Drug Approvals 2021 – Kidney Diseases

Kerendia (finerenone)

- Indication: chronic kidney disease in adult patients with type 2 diabetes

  – to reduce risk of eGFR decline, ESRD, CV death, non-fatal MI and hospitalization for heart failure

- MOA: **first-in-class** mineralocorticoid receptor antagonist; blocks sodium reabsorption overactivation in the kidneys and other tissues, which is thought to cause fibrosis and inflammation

- Dosing: 10 mg PO once daily with eGFR 25-60; 20 mg once daily if eGFR > 60
  - Avoid with eGFR < 25 or serum potassium > 5.0
  - Contraindicated with strong CYP3A4 inhibitors, adrenal insufficiency; avoid grapefruit juice
  - Monitor serum potassium (increases serum potassium twice that of placebo), serum sodium, and blood pressure (hypotension)

- FIDELIO-DKD Phase 3 clinical trial – 5674 patients with median follow-up at 2.6 years; finerenone reduced risk of composite CV outcome vs placebo (P=0.034)
  - finerenone + SGLT2 inhibitors demonstrated additive effects in improving composite CV and renal outcomes

Kerendia [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc. 2021
Circulation. 2021;143:540–552. DOI: 10.1161/CIRCULATIONAHA.120.051898

New Drug Approvals 2021 – Respiratory Disorders

Tezspire (tezepelumab-ekko)

- Indication: severe asthma, as add-on maintenance treatment in patients ≥ 12 years old; not for acute treatment of bronchospasm or status asthmaticus
  - MOA: **first-in-class**, thymic stromal lymphopoietin (TSLP) blocker
    - TSLP is a cytokine involved in the asthma inflammation cascade
    - Blocking TSLP reduces biomarkers and cytokines associated with inflammation
- Dosing: 210 mcg SC every 4 weeks (by healthcare provider)
- Navigator and Pathway – Phase 3 trials
  - 52-week trials of Tezepelumab vs placebo in 1609 patients who had history of exacerbations or hospitalizations in past 12 months, on ICS + asthma controller +/ oral corticosteroid
  - Reduction in annualized rate of asthma exacerbations (0.93 with Tezepelumab vs 2.10 with placebo, P<0.001)
  - ADEs– similar to placebo (pharyngitis, arthralgia, back pain)
- Phase 3 SOURCE trial did not meet primary outcome in reducing OCS use

Tezspire [package insert]. Thousand Oaks, CA: Amgen Inc. 2021

N Engl J Med 2021;384:1800-9. DOI: 10.1056/NEJMoa2034975

New Drug Approvals 2021 – CNS and Neurology Disorders

Aduhelm (aducanumab-avwa)

- Indication: treatment of Alzheimer's disease (AD); accelerated approval pathway (surrogate endpoints) contingent on verified benefit in confirmatory trials
- MOA: **first-in-class** antibody that binds to and reduces amyloid beta plaques
- Dosing: 10 mg/kg IV infusion over 60 min, every 4 weeks
  - Obtain brain MRI before treatment initiation, prior to 7th and 12th doses to monitor for amyloid-related imaging abnormalities (ARIA)
  - Most common ADEs: brain edema (35%), microhemorrhages (21%), headache (13%), falls
- Phase 3 Clinical trials – patients 50-85 years old with early AD (n=1093)
  - EMERGE and ENGAGE trials – conflicting results when measuring cognitive decline
    - EMERGE trial only showed benefit at high dose aducanumab
  - FDA Advisory Committee questioned evidence supporting amyloid as a valid surrogate endpoint

Aduhelm [package insert]. Cambridge, MA: Biogen. 2021
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8491638/

New Drug Approvals 2021 – CNS and Neurology Disorders

Aduhelm Controversies

- Approved Jun 2021; 3 members of the FDA panel resigned
- Dec 2021 – cost reduced from $56,000 to $28,200 per year
- Dec 2021 – EMA decided not to approve the product in the EU
- Jan 2022 - CMS said it will only provide reimbursement for patients enrolled in clinical trials that meet their criteria
- Mar 2022 - Phase 4 ENVISION confirmatory trial protocol submitted to FDA
  - Will be a global, placebo-controlled trial with approx. 1500 patients with early AD
  - Primary endpoint will be clinical dementia rating measure after 18 months of treatment; long-term extension to collect data for up to 4 years

https://www.fiercepharma.com/marketing/biogen-alzheimer-s-drug-aduhelm-cms-restrictive-draft-reimbursement-ruling-could
https://investors.biogen.com/news-releases/news-release-details/update-phase-4-confirmatory-study-aduhelmr
https://ucsdnews.ucsd.edu/pressrelease/novel-drug-prevents-amyloid-plaques-a-hallmark-of-alzheimers-disease

New Drug Approvals 2021 – ADHD

Drug	Azstarys (serdexmethylphenidate and dexmethylphenidate)	Qelbree (viloxazine)
Indication	CNS stimulant (long-acting and short-acting) for ADHD in patients ≥ 6 years old	Selective norepinephrine reuptake inhibitor (non-stimulant) for ADHD in patients 6-17 years old
Dosing	39.2mg/7.8mg PO once daily in AM titrated to 52.3mg/10.4mg PO once daily	6-11 year old: 100mg PO once daily initially; titrate to 400mg PA once daily 12-17 year old: 200mg PO once daily initially; titrate to 400mg PO once daily
ADEs	decreased appetite, insomnia, N/V, dyspepsia, abdom pain, weight decrease, anxiety, etc.	somnolence, decreased appetite, fatigue, nausea, insomnia, irritability
Warnings	severe CV reactions, BP and HR increases, psychiatric reactions, priapism, peripheral vasculopathy, long-term suppression of growth	BP and heart rate increases, activation of mania or hypomania, somnolence and fatigue
Contrain-dications	MAO-I in preceding 14 days; known sensitivity to product components	MAO-I and CYP1A2 substrates
Boxed Warnings	abuse and dependence	suicidal thoughts and behaviors

Azstarys [package insert]. Grand Rapids, MI: Corium. 2021
Qelbree [package insert]. Winchester, KY: Catalent Pharma Soluntions. 2021

New Drug Approvals 2021 – CNS and Neurology Disorders

Lybalvi (olanzapine and samidorphan)

- Once-daily, oral atypical antipsychotic, opioid antagonist combination
- Indications:
  - schizophrenia in adults
  - bipolar 1 disorder in adults – maintenance monotherapy or acute treatment of manic or mixed episodes, as monotherapy and as adjunct to lithium or valproate
- ENLIGHTEN-2 trial demonstrated less weight gain than olanzapine alone

Qulipta (atogepant)

- Once-daily oral calcitonin gene-related peptide receptor antagonist
- Indication: prevention of episodic migraine in adults
- ADVANCE trial demonstrated ≥ 50% decrease in migraines versus placebo

Lybalvi [package insert]. Waltham, MA: Alkermes. 2021

Qulipta [package insert]. Dublin, Ireland. AbbVie. 2021

New Drug Approvals 2021 – Atopic Dermatitis

Adbry (tralokinumab-ldrm)

- **First-in-class** interleukin-13 antagonist for atopic dermatitis (mod-severe) in adults
  - IL-13 cytokine is a key driver of atopic dermatitis symptoms
  - When topical therapies not advisable or controlling disease
  - Can be used with/without topical corticosteroids (TC)
- Dosing: initially 600 mg SC (4x150 mg injections), then 300 mg SC every other week
  - 300 mg every 4 weeks can be considered if patient is <100 kg and responding with clear skin after 16 weeks of treatment
- Warnings: conjunctivitis and keratitis, risk of infection with live vaccines
- ECZTRA 1, 2 and 3 Phase 3 trials
  - Efficacy outcomes – goals met with tranlokinumab $\underline{+}$ TC versus placebo:
    - 1) Global Assessment score of clear or almost clear skin at 16 weeks;
    - 2) $\underline{\geq}$ 75% improvement in the Eczema Area and Severity score;
    - 3) reduction in weekly average Worst Daily Pruritus scale $\underline{\geq}$ 4 point reduction
- Safety outcomes from 5 pooled R/DB/PC trials
  - ADEs at a higher rate than placebo: upper respiratory tract infections, conjunctivitis, injection site reactions, eosinophilia

Adbry [package insert]. Madison, NJ: LEO Pharma Inc. 2021

New Drug Approvals 2021 – Secondary Pruritis Disorders

Bylvay (odevixibat)

- **First in class**, orphan drug for pruritus in pediatric (≥ 3 months) patients with progressive familial intrahepatic cholestasis (autosomal recessive diseases)
  - MOA: non-systemic ileal bile acid transport (iBAT) inhibitor; reduces bile acids and associated pruritus
  - once-daily 40 mcg/kg; oral capsule opened and sprinkled onto soft foods
    - Signif reduction in pruritis and serum bile acids
- ADEs – can lead to fat soluble vitamin deficiencies
- Place in therapy – first non-surgical treatment for this disease; clinical trials underway for Alagille syndrome and biliary atresia

Livmarli (Maralixibat)

- Orphan breakthrough drug for cholestatic pruritus in patients (>1 year old) with Alagille syndrome, a rare liver disease
  - MOA: non-systemic ileal bile acid transport (iBAT) inhibitor
  - Once-daily oral solution taken 30 minutes before breakfast
    - Signif reduction in pruritus and serum bile acids
- Livmarli is $46,500 for a 30mL bottle and $391,000 per year; Bylvay is $385,000 per year

Bylvay [package insert]. Boston, MA: Albireo. 2021, Livmarli [package insert]. Foster City, CA. Mirum. 2021

New Drug Approvals 2021 – Secondary Pruritis Disorders

Korsuva (defelikefalin)

- **First-in-class** – kappa opioid receptor (KOR) agonist targeting the body's peripheral nervous system
- Breakthrough drug filling unmet need for mod-severe pruritus in adults undergoing hemodialysis
  - Not studied in patients on peritoneal dialysis or in patients with severe hepatic impairment
- 0.5 mcg/kg IV bolus at the end of each hemodialysis treatment
  - Administer within 60 minutes of syringe preparation
- ADEs – diarrhea, dizziness, nausea, gait disturbance, falls, hyperkalemia, headache, somnolence and mental status changes
- KALM-1 U.S. clinical trials measured reduction in scores on Worst-Itching Numerical Rating Scale (WI-NRS)
  - 49.1% in difelikefalin group had a decrease of $\geq$ 3 points vs 27.9% in placebo group (P<0.001)

Korsuva [package insert]. Stamford, CT. Cara Therapeutics Inc. 2021
N Engl J Med 2020;382:222-232. DOI:10.1056/NEJMoa1912770

New Drug Approvals 2021 – Benign Neoplastic Disorders

Welireg (belzutifan)

- **First-in-class**, orphan drug – hypoxia-inducible factor inhibitor to treat adult patients with von Hippel-Lindau (VHL) disease
  - Rare genetic disease that causes benign tumors and cysts to grow in brain, spinal cord, kidneys, pancreas, adrenal glands and reproductive tract
- 120 mg orally administered once daily until disease progression or unacceptable toxicity
- Boxed Warning: can cause embryo-fetal harm; non-hormonal contraception is required
- Warnings:
  - Anemia (90% of patients; median onset 31 days) - may require transfusions; ESAs are not recommended
  - Hypoxia (up to 29% of patients) – may require supplemental oxygen or hospitalization
- ADEs – decreased hemoglobin, anemia, fatigue, increased serum creatinine, headache, dizziness, increased glucose, nausea
- Drug interactions with UGT2B17 and CYP2C19 inhibitors – monitor for anemia and hypoxia
- Phase 3 open-label clinical trials
  - Patients with VHL renal cell carcinomas - overall response rate 49%; 56% with duration of response $\geq$ 12 months
  - Patients with VHL-associated CNS hemangiomas or pancreatic neuroendocrine tumors - overall response rate 63%/83%; 73%/50% with duration of response $\geq$ 12 months

Welireg [package insert]. Whitehouse Station, NJ. Merck Sharpe & Dohme Corp. 2021

Amondys 45 (casimersen)

- Priority, orphan drug for treatment of Duchenne muscular dystrophy (DMD)
  - DMD is due to a rare genetic mutation that prevents production of the protein dystrophin which strengthens and protects muscles
    - Progressive muscle damage and weakness; walking and breathing difficulty over time
    - One in 2500-5000 boys are born with DMD
  - Casimersen is an antisense oligonucleotide targeted to treat DMD patients amenable to exon 45 skipping (8% of DMD patients)
- Four other FDA approved drugs for DMD:
  - **Exondys 51 (eteplirsen)** – first drug for DMD – subset of patients with genetic mutation amenable to skipping exon 51 (13% of DMD patients)
  - **Vyondys 53 (golodirsen)** and **Viltepso (viltolarsen)**– subset of patients with generic mutation amenable to skipping exon 53 (8% of DMD patients)
  - **Emflaza (deflazacort)** – an oral glucocorticoid pro-drug with anti-inflammatory and immunosuppressive effects

Amondys45 [package insert]. Cambridge, MA. Sarepta Therapeutics Inc.. 2021

Amondys 45 (casimersen)

- 30 mg/kg administered once weekly via 35-60 minute IV infusion (use 0.2 micron filter)
- Warnings: kidney toxicity observed in animals; monitor kidney function
- ESSENCE Trial
  - Ongoing Phase 3 DB/PC trial
  - To evaluate efficacy and safety of casimersen over 96 weeks followed by 48 week open-label period
  - 48-week interim analysis via muscle biopsy
    - 43 patients (ages 7-13 years) randomized 2:1 to receive casimersen or placebo once weekly
    - Exon 45 skipping significantly increased in casimersen patients (P<0.001)
    - Mean dystrophin levels signif increased from baseline with casimersen (P<0.001)
    - Signif greater increase in dystrophin levels (P=0.004)
    - Increased dystrophin correlated with exon skipping (P<0.001)

Pipeline of new drugs for DMD include exon skipping and gene therapies

Amondys45 [package insert]. Cambridge, MA. Sarepta Therapeutics Inc.. 2021

New Drug Approvals 2021 – Musculo-Skeletal Disorders

Nexviazyme (avalglucosidase alfa-ngpt)

- Orphan Breakthrough Priority drug for late-onset Pompe Disease in patients 1 year and older
  - Pompe Disease – rare (approx. 3500 in the U.S.), autosomal recessive disease
    - Deficiency of acid alfa glucosidase (GAA) leads to glycogen buildup in cells in organs and tissues; progressive muscle damage, functional disabilities
    - Three sub-types – infantile-onset, non-classic infantile (around 1 year), and late-onset (later in childhood or teen years) (LOPD)
    - Symptoms of LOPD – leg weakness, muscle pain, falls, enlarged heart, breathing difficulty and infections, weight loss, fatigue, difficulty swallowing
  - Enzyme replacement therapy
    - Avalglucosidase alfa is the recombinant version of GAA with more uptake into cells compared to alglucosidase alfa (Lumizyme/Myozyme)
    - Lysosomal glycogen-specific enzyme targeting the M6P receptor to clear glycogen from muscle cells
  - IV infusion every two weeks @ 20mg/kg (wt $\geq$30kg) or 40mg/kg (<30kg)

Nexviazyme [package insert]. Cambridge, MA. Genzyme Corp.. 2021

Nexviazyme (avalglucosidase alfa-ngpt)

- Boxed warnings – hypersensitivity/anaphylaxis, infusion-related reactions, risk of acute cardiorespiratory failure
  - Premedicate with antihistamines, antipyretics +/- corticosteroids to reduce risk of infusion-associated reactions
  - Start IV infusions at 1 mg/kg/hour and increase based on dose and tolerance; total infusion duration 4-5 hours (@20mg/kg) or 7 hours (@40mg/kg)
- Comet Phase 3 R/DB trial
  - Primary outcome: avalglucosidase alfa (n=51) non-inferior to alglucosidase alfa (n=49) in change from baseline to week 49 in upright FVC% predicted
  - Key secondary outcomes: greater increases in distance covered in 6MWT and percent predicted with avalglucosidase alfa vs alglucosidase alfa

Nexviazyme [package insert]. Cambridge, MA. Genzyme Corp.. 2021

Voxzogo (vosoritide)

- **First-in-class**, orphan drug for achondroplasia in patients ≥ 5 years old with open epiphyses
  - Rare genetic mutation of FGFR3 gene causing skeletal dysplasia
    - Occurs in 1 of 25,000 live births (250,000 people worldwide)
    - 90% of cases of short stature or dwarfism
  - MOA: C-type natriuretic peptide analog – regulates the signaling pathway of FGFR3 to assist bone growth
- Dosing is weight-based (0.24-0.8 mg) once daily SC injection; continue until closure of epiphyses; not recommended if eGFR < 60 mL/min/1.73m^2
- ADEs (>10%): injection site reactions/swelling/urticaria, vomiting
- Phase 3 clinical trial – 52-week R/DB/PC in 121 patients (mean age 8.7 years)
  - 15 mcg/kg SC once daily
  - Vosoritide superior to placebo in annualized growth velocity (AGV) at week 52
  - Open-label extension – subjects with 2-year follow-up maintained AGV

Voxzogo [package insert]. Novato, CA. BioMarin Pharmaceutical Inc. 2021

Vyvgart (efgartigimod alfa-fcab)

- **First-in-class**, orphan drug for myasthenia gravis in adults who are anti-acetylcholine receptor (AChR) antibody positive
  - Chronic autoimmune disease that causes weakness in skeletal muscles worsening after periods of activity and improving after periods of rest
    - Immune system produces AChR antibodies that impair communication between nerves and muscles; severe attacks can lead to life-threatening problems with breathing and swallowing
  - MOA: efgartigimod alfa is a human IgG1 antibody fragment that binds to the neonatal Fc receptor, resulting in reduction of circulating IgG
- Dose: 10 mg/kg IV infusion over 60 minutes once weekly for 4 weeks; dilute with NS
- ADEs (≥10%)– respiratory tract infections, headache, urinary tract infections
- Phase 3 ADAPT clinical trial: 26-week R/DB/PC/MC (n=167)
  - 68% of efgartigimod alfa patients demonstrated response with activities of daily living vs 30% with placebo (P<0.0001)

Vyvgart [package insert]. Boston, MA. Argenx US Inc. 2021

New Oncology Medications

New Drug Approvals 2021 – Oncology Medications

Non-Small Cell Lung Cancer (NSCLC)

Drug	**Tepmetko (tepotinib)** Orphan/Priority	**Rybrevant (amivantamab-vmjw)** FIC/Breakthrough/Priority	**Exkivity (mobocertinib)** Orphan/Breakthrough/Priority	**Lumakras (sotorasib)** FIC/Orphan/Breakthrough/Priority
Indication	Metastatic NSCLC with MET exon 14 skipping alterations	NSCLC with EGFR exon 20 insertion mutations, metastatic or locally advanced on/after platinum-based therapy	NSCLC with EGFR exon 20 insertion mutations, after progression on or after platinum-based chemotherapy	NSCLC KRAS G12C-mutated locally advanced or metastatic, second-line after ≥1 prior systemic therapy
Clinical Trial Outcomes	ORR: 43% (n=69 tx-naïve, n=83 prev treated) Median DOR: 10.8/11.1 months	ORR: 40% (n=81) Median DOR: 11.1 months	ORR: 28% (n=114) Median DOR: 17.5 months	ORR: 36% (n=124) Median DOR: 10.0 months
Dosing	450mg PO once daily	IV infusion – weekly dose for 4 weeks (initial dose split over 2 days), then every 2 weeks	160mg PO once daily	960mg PO once daily
Considerations	Monitor LFTs and for ILD DI: avoid strong CYP3A and/or P-gp inhibitors, some P-gp substrates	Premed with antihistamine, antipyretic, glucocorticoid Monitor for infusion reactions, ILD, rash, ocular toxicity	Boxed warnings for QTc prolongation; DI with CYP3A inducers/inhibitors	DI: avoid or separate from PPI or H2 antagonist; CYP3A4 inducers/ substrates; P-gp substrates

Tepmetko [package insert]. Rockland, MA. EMD Serono, 2021
Rybrevant [package insert]. Horsham, PA. Janssen Biotech, 2021.
Exkivity [package insert]. Lexington, MA. Takeda Pharmaceuticals, 2021
Lumakras [package insert]. Thousand Oaks, CA. Amgen, 2021.

New Drug Approvals 2021 – Oncology Medications for Lymphomas

Ukoniq (umbralisib)

- Priority, orphan and breakthrough kinase inhibitor for marginal zone lymphoma (MZL), relapsed or refractory after ≥ 1 anti-CD20-based regimen; follicular lymphoma (FL), relapsed or refractory after ≥ 3 prior systemic therapy lines
  - Dosing: 800mg PO once daily
    - Monitor for infection, neutropenia, diarrhea/colitis, hepatotoxicity, severe skin reactions, allergy
- Clinical Trial Outcomes – MZL: ORR 34% (varied by MZL subtypes); DOR range 0.0, 21.8 months (median not evaluable/reached); FL: ORR 50%; Median DOR 11.1 months

Zynlonta (loncastuximab tesirine-lpyl)

- **First-in-class**, orphan, priority approval for large b-cell lymphoma, relapsed or refractory after ≥ 2 lines of systemic therapy
  - MOA: CD19-directed antibody and alkylating agent conjugate
  - Dosing: IV infusion over 30 minutes every 3 weeks
    - 0.15 mg/kg every 3 weeks for 2 cycles; then 0.075 mg/kg every 3 weeks
    - Premedicate with dexamethasone PO/IV BID for 3 days prior to chemotherapy
- Warnings – monitor for edema/effusions, myelosuppression, infections, skin reactions
- Outcomes – ORR 48.3%; Median DOR 10.3 months

Ukoniq [package insert]. Edison, NJ: TG Therapeutics. 2021; Zynlonta [package insert]. Murray Hill, NJ; ADC Therapeutics. 2021

New Drug Approvals 2021 – Lymphomas/Leukemias

Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn)

- Orphan drug for acute lymphoblastic leukemia; lymphoblastic lymphoma (patients ≥1 month) with hypersensitivity to *E.coli*-derived asparaginase
  - Component of multi-agent chemo regimens; kills cancer cells due to depletion of plasma asparaginase
  - Dosing: 25 mg/m^2 IM every 48 hours
    - Monitor bilirubin, transaminases and glucose prior to treatment, then every 2-3 weeks
    - Admin in clinical setting to monitor for hypersensitivity reactions (25%)
- Warnings: hypersensitivity, pancreatitis, thrombosis, hemorrhage, hepatotoxicity
- Clinical Trial Outcomes – 94% of patients maintained target asparaginase activity
- Provides an alternative to Erwinaze (Erwinia asparaginase) which has been in shortage since 2016

Scemblix (asciminib)

- Orphan, breakthrough kinase inhibitor for chronic myeloid leukemia after ≥ 2 TKI treatments
- Dosing: 80 mg PO daily or 40 mg PO twice daily; if patient has T3151 mutation, then 200mg PO twice daily
- Warnings – myelosuppression, pancreatic toxicity, hypertension, hypersensitivity, cardiovascular toxicity
- DI: avoid concomitant use with CYP2C9 substrates or itraconazole oral solution; monitor with CYP3A4 inhibitors, substrates, P-gp substrates
- Outcomes – 29% major molecular response (MMR) at 48 weeks (n=157) vs 13% in patients receiving active control, bosutinib (n=76); 49% MMR at 96 weeks in patients with T3151 mutation (n=45) in an open-label trial

Rylaze [package insert]. Palo Also, CA: Jazz Pharmaceuticals. 2021; Scemblix [package insert]. East Hanover, NJ; Novartis. 2021.

New Drug Approvals 2021 – Oncology Medications

Drug	Indication	Dosing	Outcomes	Considerations
Pepaxto (melphalan flufenamide) Orphan/Priority	Peptide conjugated akylating agent for multiple myeloma, relapsed or refractory after ≥ 4 lines of treatment	40mg IV over 30 minutes on day 1 of each 28-day cycle; given in combination with dexamethasone	HORIZON trial (n=97): ORR 23%, Median DOR 4.2 months	OCEAN confirmatory trial results - HR 1.104; **drug withdrawn from the U.S. market**
Fotivda (tivozanib)	Kinase inhibitor for renal cell carcinoma, after ≥ 2 systemic therapies	1.34 mg PO once daily x 21 days then 7 days off (28-day cycle)	TIVO-3 trial: ORR 18% (n=175) vs 8% with Sorafenib (n=175); Median DOR not reached vs 5.7 months with Sorafenib	Hypertension in 45% of patients, hemorrhagic events in 11%, thyroid dysfunction in 11%
Jemperli (dostarlimab-gxly)	Programmed death receptor-1 (PD-1) for mismatch repair deficient (dMMR) cancers: 1) Endometrial cancer (failed platinum-containing regimen) or 2) Solid tumors failing other treatments	500 mg every 3 weeks (doses 1-4), then 1000 mg every 6 weeks; IV infusion over 30 min	GARNET trial: **Endometrial cancer (n=71)** ORR 42.3%, 93.3% DOR ≥ 6 months; **Solid tumors (n=209)** ORR 41.6%, Median DOR ≥ 34.7 months	Infusion-related reactions, immune-mediated adverse reactions (e.g. pneumonitis, colitis, hepatitis, nephritis, etc)

Pepaxto [package insert]. Waltham, MA. Oncopeptides Inc, 2021
Fotivda [package insert]. Boston, MA. AVEO Pharmaceuticals, 2021.
Jemperli [package insert]. Research Triangle Park, NC. GlaxoSmithKline, 2021
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New Drug Approvals 2021 – Oncology Medications

Drug	Indication	Dosing	Outcomes	Considerations
Truseltiq (infigrantinib) Orphan/Priority	Kinase inhibitor for cholangiocarcinoma with FGFR2 fusion, prev treated, unresectable, metastatic	125 mg PO once daily for 21 days of 28-day cycle; reduce dose for renal or hepatic impairment	Phase 2 Clinical Trial (N=108): ORR 23%, Median DOR 5.0 months	Ocular toxicity (retinal pigment epithelial detachment); hyperphosphatemia with soft tissue mineralization
Tivdak (tisotumab vedotin-tftv) First-in-Class	Tissue factor-directed antibody and microtubule inhibitor conjugate for Cervical cancer, recurrent or metastatic	2 mg/kg IV infusion over 30 minutes every 3 weeks; max dose is 200 mg; not to be mixed with other drugs	innovaTV Phase 2 Trial (n=101): ORR 24%, Median DOR 8.3 months	Boxed warning: ocular toxicity affecting corneal epithelium and conjunctiva; Monitor for peripheral neuropathy, hemorrhage, pneumonitis, and laboratory abnormalities (decreased hemoglobin, lymphocytes, leukocytes)

Truseltiq [package insert]. Brisbane, CA. QED Therapeutics, 2021
Tivdak [package insert]. Bothell, WA. Seagen Inc, 2021.

New Drug Approvals 2021 – Oncology-Associated Products

NCCN Guidelines:

Trilaciclib may be used as a prophylactic option to decrease the incidence of chemotherapy-induced myelosuppression when administered before (prophylactic G-CSF may be administered after cycle 1) platinum/etoposide ± immune checkpoint inhibitor-containing regimens or a topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC).

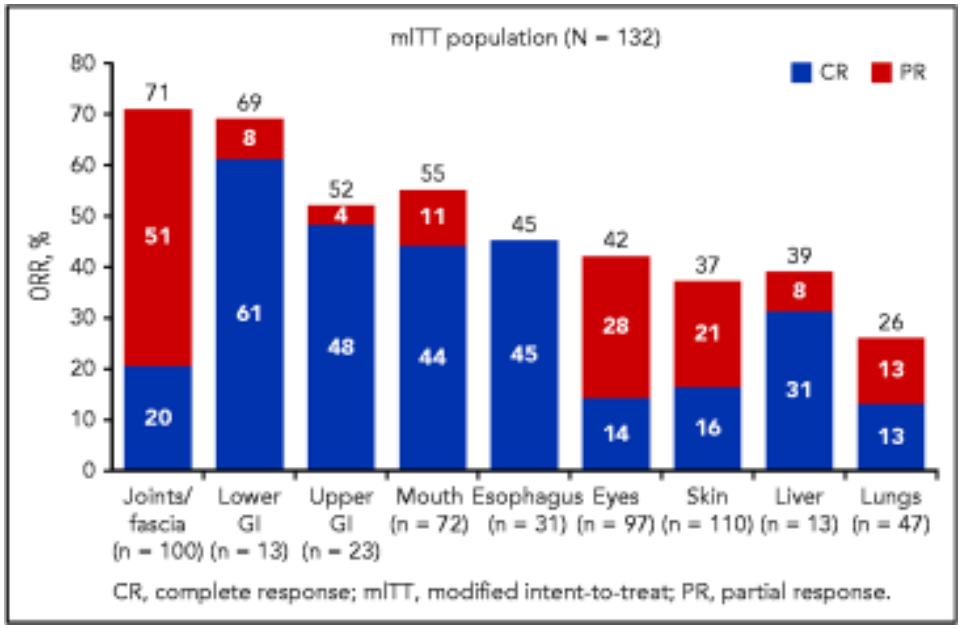
Cosela [package insert]. Durham, NC: G1 Therapeutics Inc. 2021;

New Drug Approvals 2021 – Oncology-Associated Products

Rezurock (belumosudil)

- Orphan, Breakthrough kinase inhibitor for chronic graft-versus-host disease (cGVHD), after failure of ≥ 2 lines of therapy, for patients ≥ 12 years old
  - Dosing: 200 mg PO once daily
    - Increase dose to 200 mg twice daily if patient on proton pump inhibitors or strong CYP3A inducers
- Monitor for N/V/D, infections, dyspnea, liver function test abnormalities
  - 12% of patients discontinued therapy due to ADEs
- ROCKstar Phase 2 Trial: 75% ORR (n=65) through Cycle 7; median DOR 54 weeks
- Provides an option for patients with severe cGVHD

Overall response rate by organ system in patients receiving at least one dose



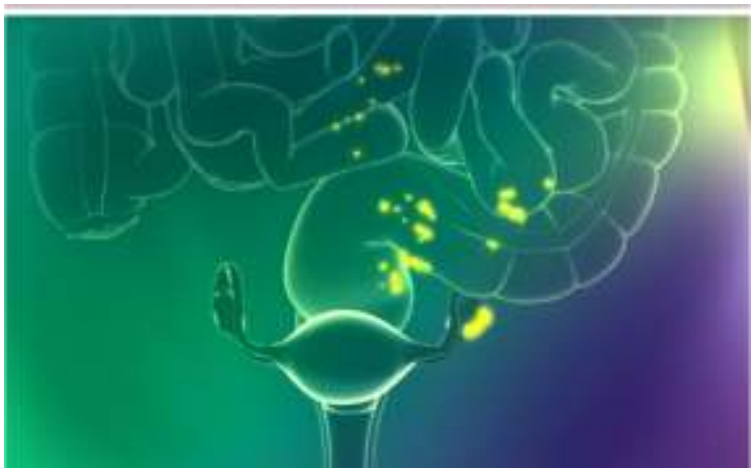
Jörg P. Halter, ROCKin' cGVHD treatment: has the time come?, Blood, 2021:138(22):2161-2162. https://doi.org/10.1182/blood.2021013186

Rezurock [package insert]. Warrendale, PA: Kadmon Pharmaceuticals. 2021

New Drug Approvals 2021 – Oncology-Associated Products

Cytalux (pafolacianine)

- **First-in-Class**, Orphan, priority imaging agent to assist in identifying ovarian cancer lesions
  - Used in intraoperative identification of malignant lesions
  - Flourescent drug that targets folate receptor – often overexpressed in ovarian cancer
- Dosing: 0.025 mg/kg IV over 60 minutes, 1-9 hours prior to surgery
  - Thaw frozen vial at room temp for at least 90 minutes
  - Shake thawed vial for 60 seconds
  - Only D5W should be used for dilution; will be light blue/green in color
  - Protect from light during infusion/storage
- Warnings: infusion-related reactions
  - Usually occur within first 15 minutes of infusion
  - treat with antihistamines and/or anti-nausea meds
- Outcomes – 27% of patients (n=134) had at least one confirmed ovarian cancer lesion detected which could not be seen under normal light or palpation



https://www.insideindianabusiness.com/articles/purdue-light-up-cancer-technology-earns-fda-approval

Cytalux [package insert]. West Lafayette, IN: On Target Laboratories, 2021

CAR-T Therapies Approved in 2021

- **Brexucabtagene Autoleucel**
  - CD19-directed CAR T product for adults with relapsed or refractory (R/R) B-cell precursor ALL
  - Previously approved for adults with R/R mantle cell lymphoma
- **Idecabtagene Vicleucel**
  - Adults with R/R multiple myeloma, after ≥ 4 lines of prior therapy
  - First B-cell maturation antigen (BCMA)-directed CAR T agent
- **Axicabtagene Ciloleucel**
  - CD19-directed CAR T product for adults with R/R follicular lymphoma, after ≥ 2 lines of therapy
- **Lisocabtagene Maraleucel**
  - CD19-directed CAR T product for adults with R/R large B-cell lymphoma, after ≥ 2 lines of therapy

https://www.targetedonc.com/view/car-t-cell-therapy-indications-grow-significantly-in-2021

New Drug Approvals 2021 – Last Four

Cabenuva (cabotegravir, rilpivirine)

- **Priority drug**
  - Co-packaged product: Cabotegravir (HIV-1 integrase strand transfer inhibitor) and rilpivirine (HIV-1 non-nucleoside reverse transcriptase inhibitor)
  - Indication: complete regimen for treatment of HIV-1 infection, for patients on a stable antiretroviral regimen with HIV-1 RNA < 50 copies/mL, without treatment failure
  - Dosing: first month – once daily PO dosing; second month – start once monthly or every other month IM dosing
    - IM administered by healthcare provider
  - FLAIR (monthly) and ATLAS (every other month) Phase 3 trials: 48-week HIV-1 RNA ≥ 50 copies/mL 1-2%
    - Every 2 months non-inferior to monthly dosing

Cabenuva [package insert]. Research Triangle Park, NC. ViiV Healthcare. 2021

Nextstellis (drospirenone, estetrol)

- Contraceptive agent
  - Drospirenone (progestin) 3 mg/tablet
  - Estetrol (estrogen) 14.2 mg/tablet
    - Native estrogen with selective actions in tissues
    - Plant-sourced
- Dosing: 28 tablet pack (24 active tablets, 4 inert); one tablet daily
  - BMI ≥ 30 kg/m^2 - less efficacy with increasing BMI
- Boxed warnings – avoid in women > 35 years who smoke; smoking increases risk of serious cardiovascular events

Nextstrella [package insert]. Greenville, NC: Mayne Pharmaceuticals, 2021

New Drug Approvals 2021 – Last Four

Pylarify (piflufloastat F 18)

- **Priority drug approval**
  - Indication: first diagnostic agent for PET imaging of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer
    - For detection of suspected metastasis and candidates for therapy
    - For detection of suspected recurrence based on elevated PSA levels
  - Dosing: 333 MBq (9 mCi) bolus IV injection, 60 minutes prior to imaging
  - ADEs: headache, dysgeusia, fatigue
  - Efficacy and safety demonstrated in OSPREY and CONDOR clinical trials

Pylarify [package insert].Billerica, MA. Progenics Pharmaceuticals, Inc. 2021

Ponvory (ponesimod)

- MOA: Sphingosine 1-phosphate receptor modulator
- Indication – Treatment of relapsing forms of multiple sclerosis
  - Including:
    - clinically isolated syndrome
    - relapsing remitting disease
    - active secondary progressive disease
- Dosing: 20 mg PO once daily
  - First dose monitoring in patients with sinus bradycardia, AV block, history of MI or heart failure
  - Avoid live attenuated vaccines during and up to 1-2 weeks after treatment initiation
- Phase 3 trial: 2-year, head-to-head trial; ponesimod superior to teriflunamide in reducing annual relapses by 30.5%

Ponvory [package insert]. Titusville, NJ: Janssen Pharmaceuticals, 2021

Audience Poll #2

Which of the following was FDA-approved as an orphan drug in 2021 for the associated disease?

A. Alzheimer's disease – Aduhelm (aducanumab-avwa)

B. ADHD -- Qelbree (viloxazine)

C. Severe asthma -- Tezspire (tezepelumab-ekko)

D. HIV-1 -- Cabenuva (cabotegravir, rilpivirine)

Audience Poll #3

First-in-class agents often provide a more focused approach to a disease state. Which of the following is **NOT** a first-in-class product that provides a potentially significant approach to a disease state?

A. Cosela (trilaciclib) for myelosuppression with certain oncology drugs

B. Livtencity (maribavir) for post-transplant CMV infection resistant to other medications

C. Ponvory (ponesimod) for relapsing forms of multiple sclerosis

D. Cytalux (pafolacianine) a fluorescent imaging agent to assist in identifying ovarian cancer lesions

Audience Poll #4

Which one of the following is **TRUE** about breakthrough drug approvals by the FDA?

A. They are guaranteed for approval at 6 months after NDA submission

B. All first-in-class drugs are considered breakthrough drugs

C. Surrogate endpoints can be used in clinical trials

D. 14 breakthrough drugs were approved in 2021: Livtencity, Cosela, Nexviazyme, Rezurock, Livmarli, Evkeeza, Jemperli, Korsuva, Lumakras, Nulibry, Rybrevant, Scemblix, Exkivity and Ukoniq

Thank you for your attention!

Any Questions?