The 2022 New Drug Academy Awards

Anthony Trovato, PharmD, MS, BCPS

Drug Information Specialist

University of Utah Health

Anthony.trovato@pharm.utah.edu

Disclosure

- Relevant Financial Conflicts of Interest
  - none
- Off-Label Uses of Medications
  - none

Learning Objectives – Pharmacists

- Differentiate between newly-approved drugs based on labeled indication(s)
- List which already-approved drugs received new labeled indications
- Distinguish which newly-approved drugs have unique administration requirements
- Identify which drugs were removed from the market in 2022 due to safety concerns

Learning Objectives – Technicians

- List which already-approved drugs received new labeled indications
- Identify which drugs were removed from the market in 2022 due to safety concerns
- Distinguish which newly-approved drugs have unique preparation requirements


AWARDS CEREMONY

Best Supporting Drug

- Nominees:
  - Maribavir
  - Mavacamten
  - Tirzepatide
  - Tabentfusp
  - Efgartigimod alfa

Maribavir (Livtencity™)

- **Labeled indication:** refractory cytomegalovirus (CMV) post-transplant in patients ≥ 12 years old and ≥ 35 kg
- **MOA:** Competitively inhibits protein kinase activity of human CMV enzyme pUL97 → inhibits phosphorylation of proteins
- **Dosage regimen:** maribavir 400 mg by mouth twice daily

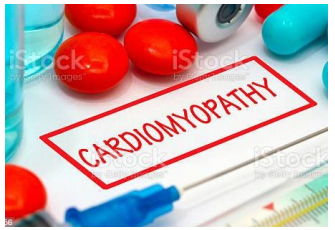
Maribavir (Livtencity™)

SOLSTICE Trial	
Population	Hematopoietic-cell and solid-organ transplant recipients (≥ 12 years old) with refractory or resistant CMV
Intervention	Maribavir 400 mg by mouth twice daily
Comparator	Investigator-assigned therapy
Outcomes	Primary: confirmed CMV clearance at end of week 8 Key secondary: CMV clearance and symptom control at end of week 8, maintained through week 16

Maribavir (Livtencity™), continued

SOLSTICE Trial Results	
Primary outcome	55.7% with maribavir vs 23.9% with investigator-assigned treatment with undetectable CMV at week 8 ($P < 0.001$)
Key secondary	18.7% patients on maribavir vs 10.3% on investigator-assigned treatment had CMV clearance and symptom control maintained through week 16 ($P = 0.01$)
Adverse reactions (> 10%)	Diarrhea, fatigue, taste disturbance, nausea, vomiting
Acute kidney injury	8.5% with maribavir vs 21.3% with foscarnet
Neutropenia	9.4% with maribavir vs 33.9% with ganciclovir/valganciclovir

Mavacamten (Camzyos™)



- **Indication:** treatment of adults with symptomatic New York Heart Association class II-III obstructive hypertrophic cardiomyopathy to improve functional capacity and symptoms
- **MOA:** cardiac myosin inhibitor that modulates myosin and actin interaction, reducing dynamic left ventricular outflow tract (LVOT) obstruction and improving cardiac filling pressures
- **Dosage regimen:** initiation and maintenance phases

Mavacamten (Camzyos™), Continued

EXPLORER-HCM Trial	
Population	Patients with hypertrophic cardiomyopathy with an LVOT gradient ≥ 50 mm Hg and NYHA class II–III symptoms
Intervention	Mavacamten 5 mg by mouth once daily, titrated to 15 mg
Comparator	Placebo by mouth once daily
Primary outcome	≥ 1.5 mL/kg/min increase in pVO2 and ≥ 1 NYHA class reduction or ≥ 3 mL/kg/min pVO2 increase without NYHA class worsening from baseline to week 30

Mavacamten (Camzyos™), Continued

EXPLORER-HCM Trial Results	
Primary outcome (overall)	45/123 (37%) patients on mavacamten vs 22/128 (17%) on placebo that met the primary endpoint (*P* = 0.0005)
≥ 1.5 mL/kg/min increase in pVO2 and ≥ 1 NYHA class reduction	41/123 (33%) patients on mavacamten vs 18/128 (14%) on placebo
≥ 3 mL/kg/min pVO2 increase without NYHA class worsening	29/123 (24%) patients on mavacamten vs 14/128 (11%) on placebo
Adverse reactions (≥ 6%)	Dizziness, syncope

Mavacamten (Camzyos™), Continued

- **Boxed warning:** reduced LVEF and risk of heart failure
- **REMS program:** echocardiograms, counseling, monitoring when starting/adjusting and throughout therapy
- Contraindications for certain drug interactions (CYP2C19 and CYP3A4)
- Restricted distribution

Tirzapetide (Mounjaro™)

- **Indication:** treatment of type 2 diabetes (T2D), as an adjunct therapy to diet and exercise in adults
- **MOA:** novel glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide 1 (GLP-1) receptor agonist
- **Dosage regimen:** subcutaneous injection once weekly
  - Start at 2.5 mg and titrate to maximum of 15 mg

Tirzapetide (Mounjaro™), Continued

SURPASS Trials	
Population	Adults with type 2 diabetes not controlled with diet and exercise alone + additional criteria per individual studies
Intervention	Tirzapatide 5 mg, 10 mg, or 15 mg subcutaneously once weekly
Comparator (SURPASS-1)	Placebo subcutaneously once weekly
Comparator (SURPASS-2)	Semaglutide 1 mg subcutaneously once weekly
Comparator (SURPASS-3)	Insulin degludec subcutaneously once daily
Comparator (SURPASS-4)	Insulin glargine subcutaneously once daily
Comparator (SURPASS-5)	Placebo subcutaneously once weekly
Outcome	Mean change in HbA1c from baseline to 40-52 weeks

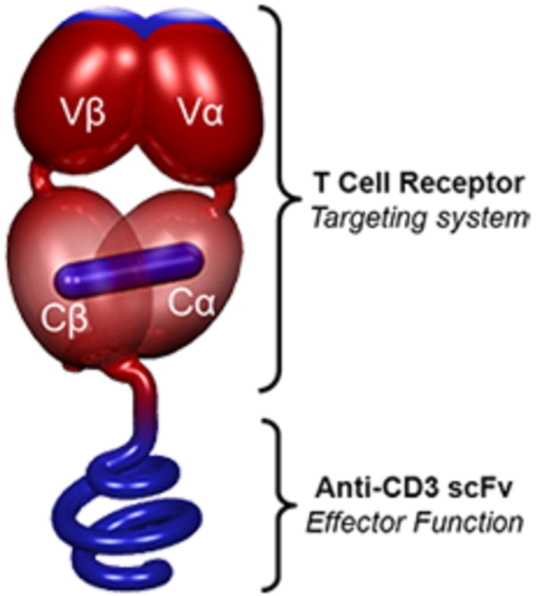
Tirzapetide (Mounjaro™), Continued

- HbA1c reductions of ~ 1.7%-2.6%
- Patients lost 12-25 pounds on average
- SURMOUNT-1
  - Mean % change in weight from baseline to 72 weeks
    - 5 mg: −15%
    - 10 mg: −19.5%
    - 15 mg: −20.9%
- Ongoing studies for weight reduction and CV outcomes

Tirzapetide (Mounjaro™), Continued

- **Adverse reactions (≥ 5%):** abdominal pain, constipation, decreased appetite, diarrhea, dyspepsia, and nausea/vomiting
- **Boxed warning:** thyroid C-cell tumors
- **Contraindications:** patients with personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2

Tebentafusp-tebn (Kimmtrak®)



- **Indication:** treatment of adults with HLA-A*02:01–positive unresectable or metastatic uveal melanoma (mUM)
- **MOA:** HLA-A*02:01-restricted T-cell receptor fused to an anti-CD3 single-chain variable → binds gp100 peptide on mUM cells, recruits and activates CD3 cells → lysis of tumor cells
- **Dosage regimen:** IV once weekly escalating doses until unacceptable toxicity or disease progression
- **Preparation:** diluted in NS + albumin

Tebentafusp-tebn (Kimmtrak®), Continued

IMCgp100-202 Trial	
Population	Previously untreated adults with HLA-A*02:01-positive metastatic uveal melanoma
Intervention	Tebentafusp-tebn IV days 1 and 8, and weekly thereafter
Comparator	Investigator choice (pembrolizumab, ipilimumab, or dacarbazine)
Primary outcome	Overall survival

Tebentafusp-tebn (Kimmtrak®), Continued

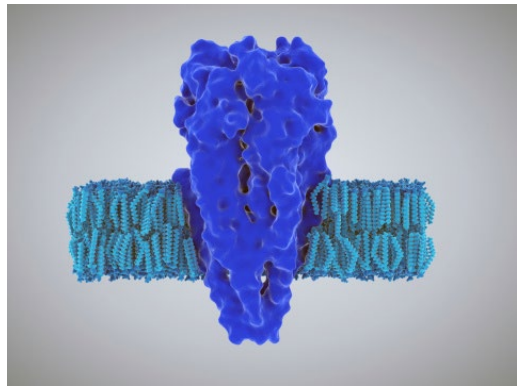
IMCgp100-202 Trial Results	
Overall survival at 1 year	73% in the tebentafusp group vs 59% in investigator choice group (HR 0.51; 95% CI, 0.37 to 0.71)
Median overall survival	21.7 months in tebentafusp group vs 16 months in investigator choice group (HR 0.51; 95% CI, 0.37–0.71)
Progression-free survival	31% in the tebentafusp vs. 19% in the investigator choice group at 6 months (HR, 0.73; 95% CI, 0.58 to 0.94)

Tebentafusp-tebn (Kimmtrak®), Continued

Safety	
Adverse reactions (≥ 30%)	Abdominal pain, chills, cytokine release syndrome, dry skin, edema, fatigue, headache, hypotension, nausea, pruritis, pyrexia, rash, vomiting
Lab abnormalities (≥ 50%)	Decreased hemoglobin, lymphocytes, or phosphate; increased AST/ALT, blood glucose, serum creatinine
Boxed warning	Cytokine-related adverse reactions • Chills (47%), hypotension (38%), and pyrexia (76%) • Monitor patients for 16 hours after first 3 infusions

Efgartigimod alfa-fcab (Vyvgart®)

- **Indication:** treatment of generalized myasthenia gravis (gMG) in adults positive for anti-acetylcholine receptor (AChR) antibodies
- **MOA:** first-in-class IgG1 antibody fragment that binds neonatal Fc receptor (FcRn) → prevents IgG from entering blood and thereby reducing overall (and AChR) IgG antibody concentrations
- **Dosage regimen:** 10 mg/kg IV once weekly for 4 weeks. Maximum dose 1,200 mg



Efgartigimod alfa-fcab (Vyvgart®), Continued

ADAPT Trial	
Population	Adults with gMG and Myasthenia Gravis Activities of Daily Living (MG-ADL) score ≥ 5 (> 50% non-ocular) on a stable dose of ≥ 1 treatment for gMg
Intervention	Efgartigimod alfa-fcab 10 mg/kg IV once weekly for 4 weeks
Comparator	Placebo IV once weekly for 4 weeks
Primary outcome	Proportion of AChR antibody-positive patients who were MG-ADL responders (≥ 2-point MG-ADL improvement sustained for ≥ 4 weeks) in the first treatment cycle

Efgartigimod alfa-fcab (Vyvgart®), Continued

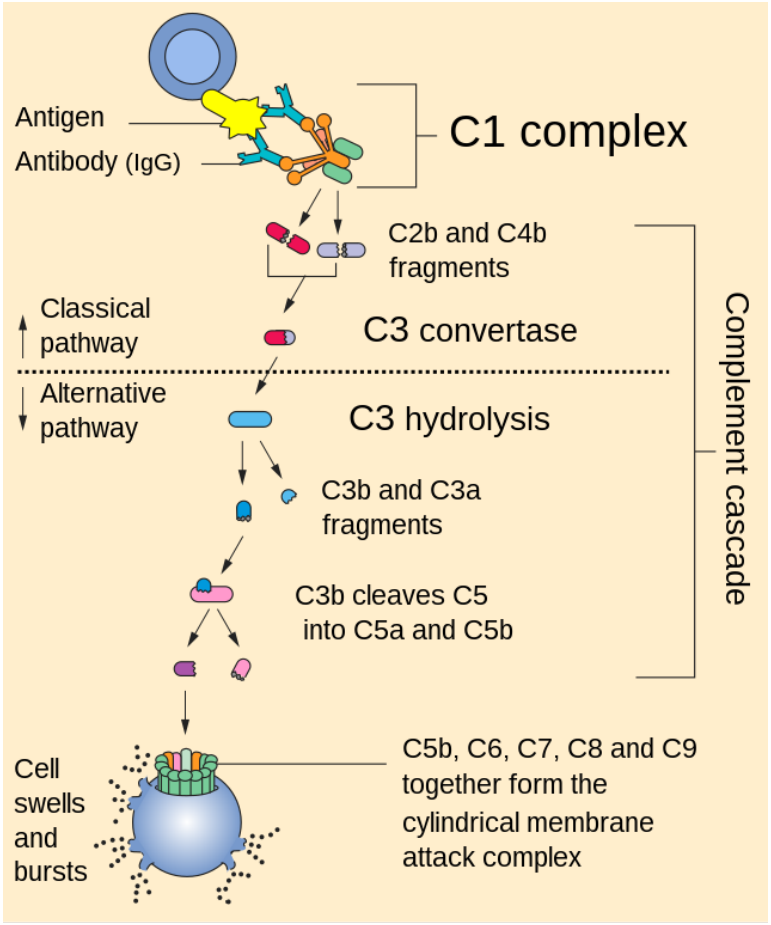
ADAPT Trial Results	
Primary outcome	44/65 (68%) acetylcholine receptor **antibody-positive patients** on efgartigimod vs 19/64 (30%) on placebo were MG-ADL responders ($P < 0.0001$)
Other outcomes	57/84 (68%) **all patients** on efgartigimod vs 31/83 (37%) on placebo were MG-ADL responders ($P < 0.0001$)
Adverse reactions (≥ 10%)	Headache, nasopharyngitis, respiratory tract infections, urinary tract infection

Best supporting drug with a new labeled indication

- Nominees:
  - Ravulizumab
  - Risankizumab
  - Dupilumab

Ravulizumab-cwvz (Ultomiris®)

- **New indication:** treatment of gMG in adults positive for AChR antibodies
- **MOA:** monoclonal antibody that binds complement protein C5, inhibiting its cleavage to C5a and C5b and preventing generation of the terminal complement complex
- **Dosage regimen:** IV loading and maintenance dosing based on body weight tiers



Ravulizumab-cwvz (Ultomiris®), Continued

CHAMPION-MG Trial	
Population	Adults with gMG and Myasthenia Gravis Activities of Daily Living (MG-ADL) score ≥ 6
Intervention	Ravulizumab IV on days 1 and 15 and every 8 weeks thereafter
Comparator	Placebo IV on days 1 and 15 and every 8 weeks thereafter
Outcome	Change in MG-ADL from baseline to 26 weeks

Ravulizumab-cwvz (Ultomiris®), Continued

CHAMPION-MG Trial Results	
Primary outcome	Mean change in MG-ADL from baseline to week 26 −3.1 in ravulizumab group vs −1.4 in placebo group ($P < 0.001$)
Adverse reactions (≥10%)	Diarrhea and upper respiratory tract infections
Boxed warning	Serious meningococcal infections
REMS	Immunization requirements, patient counseling, patient safety card requirements

Risankizumab-rzaa (Skyrizi®)

- **New indication:** treatment of moderately to severely active Crohn Disease in adults
- **MOA:** IgG1 antibody binds p19 subunit of IL-23 → inhibits prevents IL-23 from binding to receptors, preventing proinflammatory response
- 2 new dosage forms
- **Induction:** IV 600 mg at weeks 0, 4, and 8
- **Maintenance:** subcutaneous 360 mg at week 12 and every 8 weeks thereafter

Risankizumab-rzaa (Skyrizi®), continued

ADVANCE and MOTIVATE Trials	
Population	Patients 16-80 years old with moderately to severely active Crohn Disease, previously showing intolerance or inadequate response to ≥ 1 biologic or conventional therapy
Intervention	Risankizumab 600 mg or 1,200 mg IV at weeks 0, 4, and 8
Comparator	Placebo IV at weeks 0, 4, and 8
Outcome	• Clinical remission at week 12 (Crohn disease activity index (CDAI) or average daily stool frequency and abdominal pain score) • Endoscopic response at week 12 (Simple Endoscopic Score for Crohn Disease (SES-CD))

Risankizumab-rzaa (Skyrizi®), continued

ADVANCE and MOTIVATE Results	
Outcomes	All coprimary endpoints at week 12 were met in both trials with both doses of risankizumab ($P \leq 0.0001$ for all comparisons with placebo)
Adverse reactions (> 3%)	Arthralgia, headache, upper respiratory infections

Risankizumab-rzaa (Skyrizi®), continued

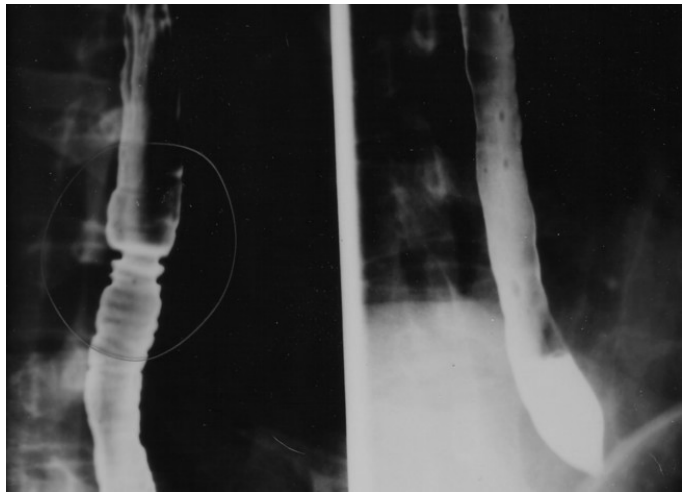
FORTIFY Trial	
Population	16-80 years with moderately to severely active Crohn's disease after risankizumab induction therapy
Intervention	Risankizumab 180 mg or 360 mg subcutaneously every 8 weeks
Comparator	Placebo subcutaneously every 8 weeks
Outcome	• Clinical remission at week 52 • Endoscopic response at week 52

Risankizumab-rzaa (Skyrizi®), continued

FORTIFY Trial Results	
Outcomes (360 mg vs placebo)	• CDAI clinical remission: 52% vs 41% (*P* = 0.0054) • Stool frequency and abdominal pain score clinical remission: 52% vs 40% (*P* = 0.0037) • Endoscopic response: 47% vs 22% (*P* < 0.001)
Outcomes (180 mg vs placebo)	• CDAI clinical remission: 55% vs 41% (*P* = 0.0031) • Stool frequency and abdominal pain score clinical remission: 46% vs 40% (*P* = 0.12) • Endoscopic response: 47% vs 22% (*P* < 0.001)
Adverse reactions (> 3%)	Abdominal pain, anemia, arthralgia, arthropathy, back pain injection site reactions, pyrexia, and urinary tract infection

Dupilumab (Dupixent®)

- **New indication:** treatment of Eosinophilic Esophagitis (EoE) ≥ 12 years old and ≥ 40 kg weight
- **MOA:** inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling and release of inflammatory cytokines and IgE by binding to the IL-4Rα subunit
- **Dosage regimen:** 300 mg subcutaneous injection once weekly



Dupilumab (Dupixent®), Continued

NCT03633617 Trial (unpublished)	
Population	Adults and adolescents with EoE
Intervention	Dupilumab subcutaneously once weekly
Comparator	Placebo
Primary outcomes	Patients with peak esophageal eosinophil counts ≤ 6 eosinophils per high-power field at 24 weeks
	Change in Dysphagia Symptom Questionnaire (DSQ) score from baseline to week 24

Dupilumab (Dupixent®), Continued

NCT03633617 Trial (unpublished)	
Population	Adults and adolescents with EoE
Intervention	Dupilumab subcutaneously once weekly
Comparator	Placebo
Primary outcomes	Patients with peak esophageal eosinophil counts ≤ 6 eosinophils per high-power field at 24 weeks
	Change in Dysphagia Symptom Questionnaire (DSQ) score from baseline to week 24

Dupilumab (Dupixent®), Continued

NCT03633617 Trial Results	
Endoscopic eosinophil counts	Part A: 60% in dupilumab group vs 5% in placebo groups achieved counts ≤ 6 eosinophils per high-power field at 24 weeks
	Part B: 59% in dupilumab group vs 6% in placebo groups achieved counts ≤ 6 eosinophils per high-power field at 24 weeks
DSQ score	Part A: mean improvement of 22 points in DSQ score in dupilumab group vs 10 points in placebo group
	Part B: mean improvement of 24 points in DSQ score in dupilumab group vs 14 points in placebo group
Adverse reactions (≥ 2%)	Herpes viral infections, injection site reactions, joint pain, and upper respiratory tract infections

In memoriam: Drugs we lost this year

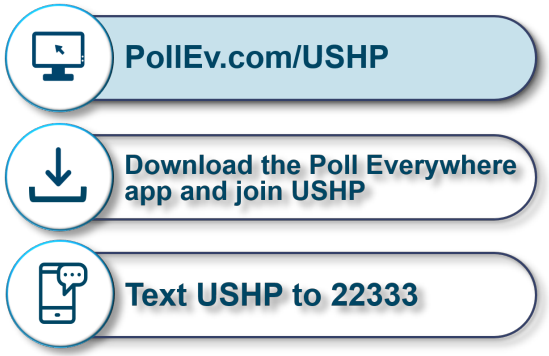
- Tegaserod (Zelnorm™)
- Umbralisib (Ukoniq®)

Audience Response Question

Pharmacists & Technicians

Which of the following drugs already on the market received new labeled indications in the past year?

A. Risankizumab-rzaa
B. Tegaserod
C. Dupilumab
D. A and C



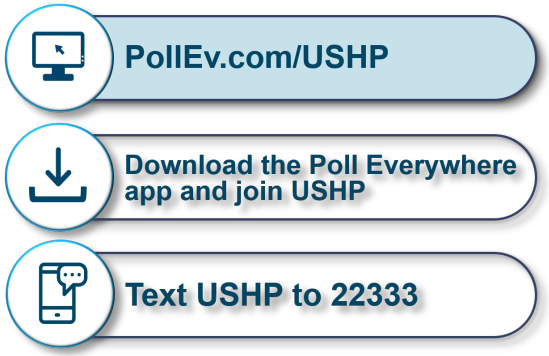
Audience Response Question

Pharmacists

For how long should staff monitor patients after administering tebentafusp-tebn?

A. For 15-20 minutes following any dose
B. For 30 minutes following any dose
C. For at least 16 hours following the first 3 doses
D. For at least 16 hours following any dose

Audience Response Question



Pharmacists

Which of the following drugs uses a patient-placed on-body injector for subcutaneous administration?

A. Efgartigimod alfa-fcab
B. Risankizumab-rzaa
C. Pegfilgrastim
D. Sutimlimab-jome

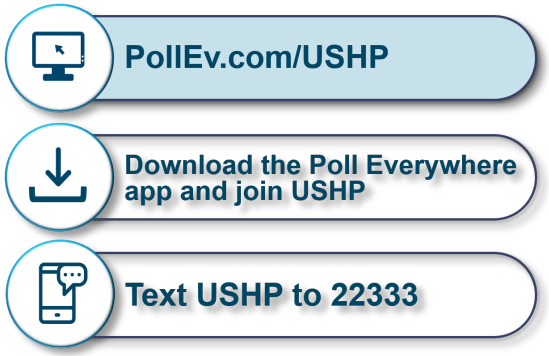
Audience Response Question

Technicians

Which of the following drugs requires dilution in an infusion bag containing albumin and 0.9% sodium chloride prior to administration?

A. Tebentafusp-tebn
B. Maribavir
C. Vutrisiran
D. Risankizumab-rzaa

Audience Response Question



Pharmacists & Technicians

Which of the following drugs were removed from the market in the past year due to safety concerns?

A. Tegaserod
B. Umbralisib
C. Maribavir
D. A and B

The 2022 New Drug Academy Awards

Anthony Trovato, PharmD, MS, BCPS
Drug Information Specialist
University of Utah Health
Anthony.trovato@pharm.Utah.edu

References

- 1 Wolters Kluwer Clinical Drug Information, Inc; 2022.
- 2 Avery RK, Alain S, Alexander BD et al. Maribavir for refractory cytomegalovirus infections with or without resistance post-transplant: Results from a phase 3 randomized clinical trial. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* 2021.
- 3 Livtencity™ [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc; 2022.
- 4 Olivotto I, Oreziak A, Barriales-Villa R et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (explorer-hcm): A randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet (London, England).* 2020; 396(10253): 759-69.
- 5 Camzyos™ [package insert]. Brisbane, CA: MyoKardia, Inc; 2022.
- 6 Dahl D, Onishi Y, Norwood P et al. Effect of subcutaneous tirzepatide vs placebo added to titrated insulin glargine on glycemic control in patients with type 2 diabetes: The surpass-5 randomized clinical trial. *Jama.* 2022; 327(6): 534-45.
- 7 Del Prato S, Kahn SE, Pavo I et al. Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (surpass-4): A randomised, open-label, parallel-group, multicentre, phase 3 trial. *Lancet (London, England).* 2021; 398(10313): 1811-24.
- 8 Frías JP, Davies MJ, Rosenstock J et al. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. *The New England journal of medicine.* 2021; 385(6): 503-15.

References

- 9 Ludvik B, Giorgino F, Jódar E et al. Once-weekly tirzepatide versus once-daily insulin degludec as add-on to metformin with or without sglt2 inhibitors in patients with type 2 diabetes (surpass-3): A randomised, open-label, parallel-group, phase 3 trial. *Lancet (London, England).* 2021; 398(10300): 583-98.
- 10 Rosenstock J, Wysham C, Frías JP et al. Efficacy and safety of a novel dual gip and glp-1 receptor agonist tirzepatide in patients with type 2 diabetes (surpass-1): A double-blind, randomised, phase 3 trial. *Lancet (London, England).* 2021; 398(10295): 143-55.
- 11 Mounjaro™ [package insert]. Indianapolis, IN: Lilly USA, LLC; 2022.
- 12 Howard JF, Jr., Bril V, Vu T et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (adapt): A multicentre, randomised, placebo-controlled, phase 3 trial. *The Lancet. Neurology.* 2021; 20(7): 526-36.
- 13 Vyvgart® [package insert]. Boston, MA: argenx US, Inc; 2022.
- 14 Nathan P, Hassel JC, Rutkowski P et al. Overall survival benefit with tebentafusp in metastatic uveal melanoma. *The New England journal of medicine.* 2021; 385(13): 1196-206.
- 15 Kimmtrak® [package insert]. Conshohocken, PA: Immunocore Commercial LLC; 2022.
- 16 Dupixent® [package insert]. Terrytown, NY: Regeneron Pharmaceuticals, Inc; 2022.

References

- 16 Dupixent® [package insert]. Terrytown, NY: Regeneron Pharmaceuticals, Inc; 2022.
- 17 D'Haens G, Panaccione R, Baert F et al. Risankizumab as induction therapy for crohn's disease: Results from the phase 3 advance and motivate induction trials. *Lancet (London, England).* 2022; 399(10340): 2015-30.
- 18 Ferrante M, Panaccione R, Baert F et al. Risankizumab as maintenance therapy for moderately to severely active crohn's disease: Results from the multicentre, randomised, double-blind, placebo-controlled, withdrawal phase 3 fortify maintenance trial. *Lancet (London, England).* 2022; 399(10340): 2031-46.
- 19 Skyrizi® [package insert]. North Chicago, IL: AbbVie Inc; 2022.
- 20 Vu T, Meisel A, Mantegazza R et al. Terminal complement inhibitor ravulizumab in generalized myasthenia gravis. 2022; 1(5): EVIDoa2100066.
- 21 Center for Drug Evaluation and Research. Ukoniq (umbralisib): Drug safety communication - fda approval of lymphoma medicine is withdrawn due to safety concerns. https://www.fda.gov/safety/medical-product-safety-information/ukoniq-umbralisib-drug-safety-communication-fda-approval-lymphoma-medicine-withdrawn-due-safety (accessed 2022 August 29).
- 22 Park B. Ibs-c treatment zelnorm withdrawn from the market again. https://www.empr.com/home/news/safety-alerts-and-recalls/ibs-c-treatment-zelnorm-withdrawn-from-the-market-again/ (accessed 2022 August 29).