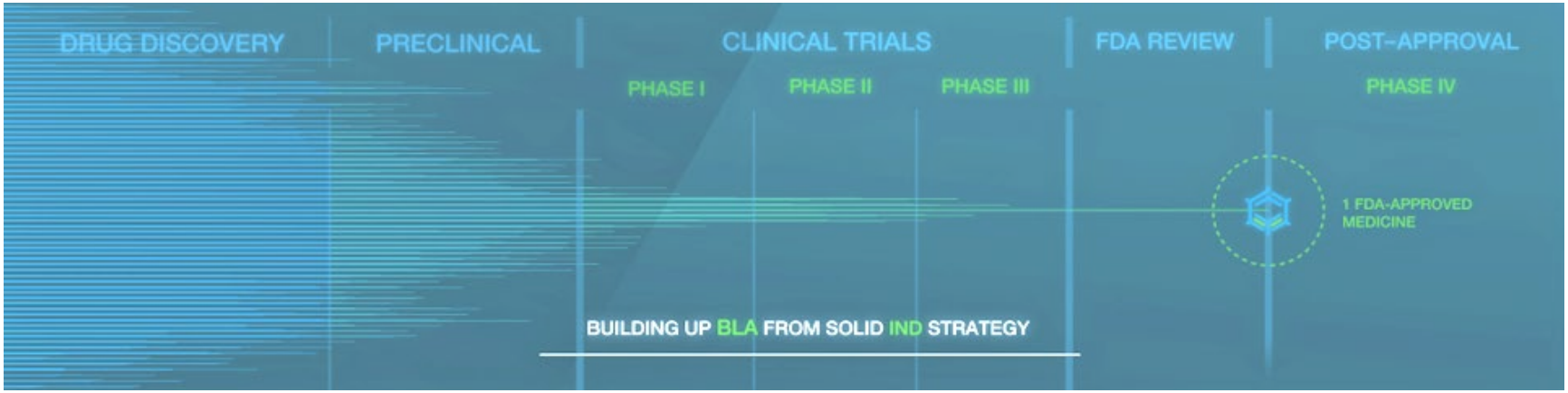
BLA REGULATORY

2020 End of the Year Summary Report-1

FDA Approved 38 New Small Molecule Drugs



BLA Regulatory, LLC (Gaithersburg, MD) provides the executive summary of the 38 new Small Molecule (SM) drugs approved by FDA in 2020 in this Year-End-Report-1. Reviewers/Readers are suggested to open FDA links for detailed information and accuracy.

Number of approved SM drugs in sub-categories

Therapeutic Area		Formulation		Regulatory Program	
Oncology	13	Tablet	14	Accelerated Approval	1
Neurology	7	IV Solution	11	EUA	1
Infection	6	Capsule	7	Fast Track	1
Metabolic disease	4	Other oral forms	3	Orphan Drug	20
GI Disease	2	Topical cream	3	Priority Review	20
Genetic disorder	2				
Dermatology and other	3				
Hematology	1				

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
1	Ayvakit (avapritinib) Tablet	Blueprint	To treat adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.	PDGFRA	Orphan Drug	The safety and efficacy of AYVAKIT for the treatment of GIST were evaluated in one trial. This was a multicenter, open-label, single-arm trial in adult patients with unresectable or metastatic GIST, harboring a PDGFRA exon 18 mutation. AYVAKIT was administered orally once daily (300 mg or 400 mg) until disease progression or unacceptable toxicity. The primary endpoint was overall response rate (ORR), defined as the proportion of patients who achieved either a complete or partial response. ORR was based on disease assessment by independent radiological review using modified RECIST v1.1 criteria, in which lymph nodes and bone lesions were not targeted lesions and progressively growing new tumor nodules within a pre-existing tumor mass progressed. An additional efficacy outcome measure was the duration of response (DOR).	FDA link	1/9
2	TAZVERIK (tazemetostat) Tablet	Epizyme, Inc.	Treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection	EZH2	Accelerated Approval, Orphan Drug	The safety and efficacy of TAZVERIK were established in an open-label, single-arm cohort (Cohort 5) of a multi-center trial in patients with histologically confirmed, metastatic, or locally advanced epithelioid sarcoma. Patients received TAZVERIK 800 mg orally twice daily until disease progression or unacceptable toxicity. The efficacy outcome measures were confirmed ORR according to RECIST v1.1 as assessed by BICR and DOR.	FDA Link	1/23
3	PIZENSY (lactitol) Powder for oral solution	Braintree Laboratories, Inc.	Treatment of chronic idiopathic constipation (CIC) in adults	82934008 chronic idiopathic constipation	Standard	The safety and efficacy of PIZENSY were established in a randomized, double-blind, placebo-controlled trial of 6 months duration. All patients had less than 3 bowel movements per week and at least one additional constipation-related symptom for at least 12 weeks (which need not be consecutive) in the preceding 12 months. Patients received either 20 g of PIZENSY or placebo daily. Patients who develop persistent diarrhea or loose stools could reduce their dose to 10 g of PIZENSY daily. The primary efficacy outcome measure was the proportion of patients who achieved at least 3 complete spontaneous bowel movements (CSBMs) in a given week and an increase of at least 1 CSBM from baseline in the same week for at least 9 weeks out of the 12-week treatment period. Additionally, two trials provided supportive evidence: 1. an active control, double-blinded, double-dummy trial of three months duration utilizing the same endpoint 2. an uncontrolled safety trial of one-year duration.	FDA Link	2/12

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
4	NEXLETOL (bempedoic acid) Tablets	Esperion Therapeutics, Inc	Treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C	cholesterol	Standard	The efficacy and safety of NEXLETOL were investigated in two similarly designed multi-center, randomized, double-blind, placebo-controlled trials that enrolled adult patients with HeFH and/or ASCVD. All patients were receiving a maximally tolerated dose of a statin, with or without other lipid-lowering therapies, and maintained a low cholesterol diet. Patients were randomized 2:1 to NEXLETOL or placebo tablets daily. The trials evaluated the percent change in LDL-C from baseline to week 12 as the primary endpoint.	FDA Link	2/21
5	BARHEMSYS® (amisulpride) IV infusion	Acacia Pharma Ltd	In adults for: 1. Prevention of postoperative nausea and vomiting (PONV), either alone or in combination with an antiemetic of a different class. 2. Treatment of PONV in patients who have received antiemetic prophylaxis with an agent of a different class or have not received prophylaxis.	PONV	Standard	Four trials provided data for efficacy and safety assessments of BARHEMSYS. BARHEMSYS for the prevention of PONV was evaluated in two randomized, double-blind, placebo-controlled, multi-center trials in patients undergoing general anesthesia and elective surgery (Trial 1 and Trial 2). In Trial 1, patients received monotherapy with BARHEMSYS; while in Trial 2, patients received BARHEMSYS in combination with one other intravenously administered, non-dopaminergic antiemetic (ondansetron, dexamethasone or betamethasone). In both trials, patients were administered BARHEMSYS at the induction of anesthesia. The primary efficacy endpoint was Complete Response, defined as an absence of any episode of vomiting or use of rescue medication within the first 24 hours postoperatively. BARHEMSYS for the treatment of PONV was evaluated in two randomized, double-blind, placebo-controlled, multi-center trials in patients experiencing PONV after general anesthesia and elective surgery (Trial 3 and Trial 4). Trial 3 enrolled patients who had not received prior PONV prophylaxis, whereas Trial 4 included patients who had received and failed PONV prophylaxis with an antiemetic of another class. The primary efficacy endpoint was Complete Response, defined as an absence of any episode of vomiting or use of rescue medication within the first 24 hours after treatment (excluding vomiting within the first 30 minutes).	FDA Link	2/26
6	NURTEC ODT (rimegepant) orally disintegrating tablets	Biohaven Pharmaceutical Inc.	The acute treatment of migraine with or without aura in adults	CGRP	Priority Review	The efficacy and safety of NURTEC ODT were evaluated in one randomized, placebo-controlled, double-blinded trial of patients with migraine headaches with or without aura.Patients were instructed to treat a migraine with moderate to severe headache pain intensity with one dose of trial medication (NURTEC ODT or placebo). Rescue medication (i.e., NSAIDs, acetaminophen, and/or an antiemetic) was allowed 2 hours after the initial treatment. The primary efficacy endpoints were pain freedom and most bothersome symptom (MBS) freedom at 2 hours post-dose.	FDA Link	2/27

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
7	ISTURISA (osilodrostat) Tablets	Novartis	The treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative	CYP11B1 enzyme	Orphan Drug designation	The safety and efficacy of ISTURISA were evaluated in a multicenter, 48-week trial that enrolled Cushing's disease patients with persistent or recurrent disease despite pituitary surgery or de novo patients for whom surgery was not indicated or who had refused surgery. The trial consisted of four periods as follows: 1. Period 1: 12-week, open-label, dose-titration period 2. Period 2: 12-week, open-label, maintenance treatment period 3. Period 3: 8-week, double-blind, placebo-controlled, randomized withdrawal treatment period which provided the data for the primary efficacy endpoint 4. Period 4: open-label treatment period of 14 to 24 weeks duration The primary efficacy endpoint was the percentage of complete responders at the end of the 8- week randomized withdrawal period (Period 3) between patients randomized to continue ISTURISA versus the patients switched to placebo. A complete responder for the primary endpoint was defined as a patient who had mUFC ≤ ULN based on central laboratory results at the end of Period 3 (Week 34), and who neither discontinued randomized treatment or the study nor had any dose increase above their Week 26 dose. The key secondary endpoint was a complete responder rate after the first 24 weeks of treatment with ISTURISA.	FDA Link	3/6
8	ZEPOSIA® (ozanimod) Capsules	Celgene Corporation	Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults	S1P1	Standard	The safety and efficacy of ZEPOSIA were established in two randomized, double-blind, double-dummy, active comparator-controlled clinical trials of similar design. Both trials included patients with relapsing forms of multiple sclerosis (MS). Patients were randomized to receive either ZEPOSIA 0.92 mg or 0.46 mg given orally once daily, beginning with a dose titration or interferon (IFN) beta-1a, 30 mcg given intramuscularly once weekly. Patients in Trial 1 were treated until the last enrolled patient completed 1 year of treatment and patients in Trial 2 were treated for 2 years. The primary endpoint was the annualized relapse rate (ARR) during the treatment period. Additional outcome measures included: 1) the number of new or enlarging MRI T2 hyperintense lesions over 12 and 24 months, 2) the number of MRI T1 Gadolinium-enhancing (Gd+) lesions at 12 and 24 months, and 3) the time to confirmed disability progression, defined as at least a 1-point increase from baseline EDSS confirmed after 3 months and after 6 months.	FDA Link	3/25

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
9	KOSELUGO (selumetinib) Capsules	AstraZeneca Pharmaceuticals LP	The treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN).	MAP2K1, MAP2K2	Priority Review, Orphan Drug designation	The efficacy and safety of KOSELUGO were evaluated in an open-label, multicenter, single-arm trial (SPRINT Phase II Stratum 1, NCT01362803). Eligible patients were required to have NF1 with inoperable PN, defined as a PN that could not be completely removed without risk for substantial morbidity due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN. Patients received KOSELUGO 25 mg/m2 orally twice daily until disease progression or unacceptable toxicity. The major efficacy outcome measure was ORR, defined as the percentage of patients with complete response (defined as disappearance of the target PN) or confirmed partial response (defined as ≥ 20% reduction in PN volume confirmed at a subsequent tumor assessment within 3 6 months). An additional efficacy outcome measure was DoR.	FDA Link	4/10
10	TUKYSA™ (tucatinib) Tablets	Seattle Genetics, Inc.	Treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.	ERBB2	Priority Review, Orphan Drug designation	There was one trial that provided data for approval of TUKYSA. Enrolled patients were required to have HER2-positive, unresectable locally advanced or metastatic breast cancer, with or without brain metastases, and had prior treatment with trastuzumab, pertuzumab, and ado-trastuzumab emtansine (T-DM1) separately or in combination, in the neoadjuvant, adjuvant or metastatic setting. Patients received TUKYSA 300 mg or placebo, orally twice daily, in combination with a trastuzumab loading dose of 8 mg/kg on Day 1 of Cycle 1 if needed and then a maintenance dose of 6 mg/kg on Day 1 of every 21-day cycle, and capecitabine 1000 mg/m2 orally twice daily on Days 1 through 14 of every 21-day cycle. An alternate trastuzumab dosing regimen was 600 mg administered subcutaneously on Day 1 of every 21-day cycle. Patients were treated until disease progression or unacceptable toxicity. Tumor assessments, including brain-MRI in patients with presence or history of brain metastases at baseline, occurred every 6 weeks for the first 24 weeks and every 9 weeks thereafter. The major efficacy outcome measure was progression-free survival (PFS) in the first 480 randomized patients assessed by blinded independent central review (BICR) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Additional efficacy outcome measures were evaluated in all randomized patients and included overall survival, PFS among patients with a history or presence of brain metastases, and confirmed objective response rate (ORR).	FDA Link	4/17

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
11	PEMAZYRE™ (pemigatinib) Tablets	Incyte Corporation	The treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangements as detected by an FDA-approved test.	FGFR1, FGFR2, FGFR3	Priority Review, Orphan Drug designation	There was one multi-center, open-label, single-arm trial that provided data for approval of PEMAZYRE.Enrolled patients were required to have locally advanced unresectable or metastatic cholangiocarcinoma whose disease had progressed on or after at least one prior therapy, and an FGFR2 gene fusion or other rearrangements.Patients received PEMAZYRE in 21-day cycles at a dosage of 13.5 mg orally once daily for 14 consecutive days, followed by 7 days off therapy. PEMAZYRE was administered until disease progression or unacceptable toxicity.The major efficacy outcome measures were overall response rate (ORR) and duration of response (DoR) as determined by an independent review committee (IRC) according to RECIST v1.1.	FDA Link	4/17
12	ONGENTYS (opicapone) Capsules	Neurocrine Biosciences, Inc.	As a catechol-O-methyltransferase (COMT) inhibitor indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.	COMT	Standard	The safety and efficacy of ONGENTYS as the adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes was evaluated in two randomized, multicenter, double-blind, 12-week placebo-controlled trials. Patients enrolled in the trials had been treated with levodopa/DOPA decarboxylase inhibitor (DDCI) (alone or in combination with other PD medications) and continued their treatment during the trials following randomization to ONGENTYS or placebo. The trials measured the change mean absolute off-time based on 24-hour patient diaries completed 3 days prior to each of the scheduled visits.	FDA Link	4/24
13	TABRECTA™ (capmatinib) Tablets	Novartis Pharmaceuticals Corporation	The treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test.	MET	Priority Review, Orphan Drug designation	There was one multicenter, non-randomized, open-label, multi-cohort study that provided data to evaluate the safety and the efficacy of TABRECTA for patients with metastatic NSCLC with a mutation that leads to MET exon 14 skipping. Patients received TABRECTA 400 mg orally twice daily until unacceptable toxicity or disease progression. The major efficacy outcome measures were overall response rate and duration of response as determined by a blinded independent review committee according to RECIST v1.1. Safety assessment was done on all patients who received at least one dose of TABRECTA.	FDA Link	5/6
14	RETEVMO™ (selpercatinib)	Eli Lilly and Company	The treatment of RET fusion-positive non-small cell lung cancer in	RET	Priority Review,	There was one multicenter, open-label, multi-cohort trial that provided data to evaluate the safety and the efficacy of RETEVMO for patients with advanced or metastatic RET fusion-positive cancer.	FDA Link	5/8

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
	Capsules		adult patients. Selpercatinib is also indicated for the systemic treatment of advanced or metastatic RET-mutant medullary thyroid cancer and the systemic treatment of RET fusion-positive radioactive iodine-refractory thyroid cancer in both adult and pediatric patients aged 12 and over.		Orphan Drug designation	The efficacy of RETEVMO for metastatic RET fusion-positive NSCLC was evaluated in adult patients previously treated with platinum chemotherapy and in treatment-naïve patients. The efficacy of RETEVMO for advanced or metastatic RET-mutant MTC was evaluated in patients who had been previously treated with cabozantinib, vandetanib or both, and patients who had not received prior treatment with cabozantinib or vandetanib. The efficacy for RET fusion-positive thyroid cancer was evaluated in adults and pediatric patients who were radioactive iodine-refractory (RAI, if an appropriate treatment option) and had received another prior systemic treatment, and in patients with RET fusion-positive thyroid cancer who were RAI-refractory and had not received any additional therapy. Patients received RETEVMO orally twice daily until unacceptable toxicity or disease progression. The major efficacy outcome measure for all cohorts was overall response rate and the additional measure was the duration of response as determined by a blinded independent review committee according to RECIST v1.1. Safety assessment was done on all patients who received at least one dose of RETEVMO.		
15	QINLOCK™ (ripretinib) Tablets	Deciphera Pharmaceuticals, Inc	The treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib	KIT, PDGFRA	Priority Review, Orphan Drug designation	The safety and efficacy of QINLOCK for the treatment of GIST were primarily evaluated in one trial. This was a multicenter, randomized, double-blind, placebo-controlled trial in adult patients with unresectable or metastatic GIST who had received prior treatment with imatinib, sunitinib, and regorafenib. QINLOCK 150 mg or placebo were administered orally once daily until disease progression or unacceptable toxicity. Tumor response assessments were performed every 28 days through for the first four months and then every 56 days thereafter. The primary endpoint was PFS based on disease assessment by BICR using modified RECIST 1.1 criteria. Additional efficacy outcome measures included objective response rate (ORR) by BICR and overall survival (OS).	FDA Link	5/15
16	CERIANNA™ (fluoroestradiol F 18) Intravenous injection	Zionexa-US Corporation	A radioactive diagnostic agent indicated for use with positron emission tomography (PET) imaging for the detection of estrogen receptor (ER)-positive lesions as a 17	Estrogen receptor alpha; Estrogen receptor beta	Standard	The ability of CERIANNA imaging to detect ER-positive non-primary breast cancer lesions was evaluated based on the published results from two clinical trials in women with histologically confirmed invasive breast cancer.Trial 1 (Chae et al. 2019) was a prospective, non-randomized, single-center trial. Three image readers were blinded to all clinical information, except for the location of the largest biopsied lesion, for which pathologists independently provided an Allred score (0 to 8). The image readers scored the intensity of FES uptake on a three-point scale relative to normal biodistribution as either “decreased,” “equivocal,” or “increased” (1 to 3). Image reader performance for distinguishing between ER-positive and ER-negative FES uptake was compared to biopsy.Trial 2 (Peterson et al. 2014)	FDA Link	5/20

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
			adjunct to bio18psy in patien19ts with recurrent20 or metastatic breast cancer			was a single-center study that evaluated the agreement between FES PET and biopsy results.1 Chae, SY, SH Ahn, SB Kim, S Han, SH Lee, SJ Oh, SJ Lee, HJ Kim, BS Ko, JW Lee, BH Son, J Kim, JH Ahn, KH Jung, JE Kim, SY Kim, WJ Choi, HJ Shin, G Gong, HS Lee, JB Lee, and DH Moon Diagnostic accuracy and safety of 16 alpha-[(18)F]fluoro-17beta-oestradiol PET-CT for the assessment of estrogen receptor status in recurrent or metastatic lesions in patients with breast cancer: a prospective cohort study, Lancet Oncol 2019; 20(4):546-555.2 Peterson, LM, BF Kurland, EK Schubert, JM Link, VK Gadi, JM Specht, JF Eary, P Porter, LK Shankar, DA Mankoff, and HM Linden, 2014, A phase 2 study of 16alpha-[18F]-fluoro-17betaestradiol positron emission tomography (FES-PET) as a marker of hormone sensitivity in metastatic breast cancer (MBC), Mol Imaging Biol 2014; 16(3):431-440.		
17	ARTESUNATE Intravenous injection	Amivas, LLC	The initial treatment of severe malaria in adult and pediatric patients. Treatment of severe malaria with Artesunate for Injection should always be followed by a complete treatment course of an appropriate oral antimalarial regimen.	Malaria protein EXP-1	Priority Review, Orphan Drug designation	The safety and efficacy of ARTESUNATE were established in a randomized, open-label, multicenter trial. Hospitalized patients with severe malaria were treated intravenously with either ARTESUNATE or quinine. ARTESUNATE was administered at 2.4 mg/kg IV at 0, 12 and 24 hours and then every 24 hours until the patient could tolerate oral medication. Quinine was given IV at 20 mg/kg over 4 hours, followed by 10 mg/kg over 2 to 8 hours, 3 times daily until oral therapy could be started. The endpoint was the in-hospital mortality rate. Additional supportive evidence for efficacy was obtained from a published, large international, randomized, open-label, multicenter trial comparing parenteral ARTESUNATE to parenteral quinine in pediatric patients (< 15 years of age) with severe malaria. The endpoint was the in-hospital mortality rate.	FDA Link	5/26
18	TAUVID™ (flortaucipir F 18 injection) Intravenous injection	Avid Radiopharmaceuticals, Inc.	A radioactive diagnostic agent indicated for positron emission tomography (PET) imaging of the brain to estimate the density and distribution of aggregated tau neurofibrillary tangles (NFTs) in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD).	NFTs	Priority Review	The ability of TAUVID imaging to estimate the density and distribution of NFTs was evaluated in two clinical trials. Trial 1 enrolled 156 terminally ill patients who agreed to undergo TAUVID imaging and to participate in a postmortem brain donation program. In 64 of these patients (14 with normal, 1 with mild cognitive impairment and 49 with dementia), reader interpretation of the TAUVID scan was compared to tau pathology based on scoring provided by independent pathologists, who evaluated the density and distribution of NFTs in the post-mortem brain. Trial 2 included the same terminally ill patients as in Trial 1 (plus 18 additional terminally ill patients) and 159 patients with cognitive impairment being evaluated for AD. Inter-reader agreement for five new TAUVID readers was evaluated using Fleiss' kappa statistic in all 241 patients. The exploratory analysis evaluated inter-reader agreement in two subgroups: terminally ill patients and in the AD indicated population. The safety of TAUVID was evaluated in 19 trials across the drug development program.	FDA Link	5/28

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
19	ZEPZELCA ™ (lurbinectedin) Intravenous injection	Pharma Mar USA, Inc.	The treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy	DNA	Priority Review, Orphan Drug designation	ZEPZELCA was approved based on data from the cohort of adult patients with small cell lung cancer (SCLC) whose disease progressed on or after platinum-based chemotherapy. This was part of a multicenter, open-label trial. Patients received ZEPZELCA 3.2 mg/m2 by intravenous infusion every 3 weeks (one cycle) until unacceptable toxicity or disease progression. The major efficacy outcome measure was confirmed investigator-assessed overall response rate (ORR). Additional efficacy outcome measures included duration of response (DoR), and an Independent Review Committee (IRC) assessed ORR using Response Evaluation Criteria in Solid Tumors (RECIST v1.1).	FDA Link	6/15
20	DOJOLVI™ (triheptanoin) Oral preparations	Ultragenyx Pharmaceutical Inc.	The treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD).		Orphan Drug designation	The FDA efficacy of DOJOLVI was established in a 4-month double-blind, randomized, controlled trial (Trial 3) comparing triheptanoin (7-carbon chain fatty acid) with trioctanoin (8-carbon chain fatty acid). The trial enrolled adult and pediatric patients with a confirmed diagnosis of LC-FAOD. After 4 months, patients in both groups were compared for both cardiac function and metabolic stability as assessed by clinical exam, cardiac imaging and laboratory testing of markers of blood metabolism and muscle breakdown. Safety evaluation was based on data from two additional trials. Trial 1 was a phase 2, single-arm, multicenter, prospective study to evaluate the impact of triheptanoin in patients 6 years of age and older who had been previously diagnosed with serious clinical manifestations of LC-FAOD despite current management. Patients were treated for up to 78 weeks. Trial 2 was an open-label, single-arm, multicenter trial in patients who rolled over from previous commercial or investigator-sponsored trials using triheptanoin or in patients who were triheptanoin treatment-naïve. The patients were to be evaluated every 3 months for up to 5 years. The trial is currently ongoing.	FDA Link	6/30

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21	BYFAVO™ (remimazolam) Intravenous injection	Acacia Pharma	The induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less.	GABA(A) Receptor	Standard	FDA approved BYFAVO based on three, randomized, double-blind, multi-center trials conducted in adult patients receiving procedural sedation.Trials 1 and 2 were conducted in American Society of Anesthesiologists Physical Status (ASA PS) class I to III patients undergoing colonoscopy or bronchoscopy, respectively. BYFAVO 5 mg (2 mL) i.v. was administered as an initial bolus, followed by 2.5 mg (1 mL) top-up doses versus placebo 2 mL administered as an initial bolus, followed by 1 mL top-up doses. Midazolam rescue was dosed per investigator discretion in both treatment groups. Fentanyl was administered as an analgesic pre-treatment at an initial dose of 50 to 75 mcg i.v. (or a reduced dose for debilitated patients) immediately prior to administration of the initial dose of study medication.The primary efficacy endpoint for BYFAVO versus placebo in both trials was the success of the procedure, defined as a composite of the following:1. Completion of the procedure, and2. No requirement for a rescue sedative medication, and3. No requirement for more than 5 doses of study medication within any 15-minute window.Trial 3 was conducted in ASA PS class III and IV patients undergoing colonoscopy. BYFAVO 2.5 mg (1 mL) to 5 mg (2 mL) i.v. was administered as an initial bolus, followed by 1.25 mg (0.5 mL) to 2.5 mg (1 mL) top-up doses versus placebo 1 to 2 mL administered with midazolam rescue, dosed per investigator discretion. Fentanyl was administered as an analgesic pre-treatment at an initial maximum dose of 50 mcg (with dose reduction for debilitated patients), immediately prior to administration of the initial dose of study medication. The primary objective of this trial was to assess the safety of multiple doses of BYFAVO compared to placebo and midazolam. Procedure success was a secondary objective.	FDA Link	7/2
22	RUKOBIA (fostemsavir) Tablets	ViiV Healthcare	The treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations	Envelope glycoprotein gp160	Priority Review	FDA approved RUKOBIA based on data from one partially randomized, double-blind, placebo-controlled, international, multicenter trial conducted in heavily treatment-experienced adult patients. In the randomized cohort, patients received either RUKOBIA or placebo twice daily in addition to their current failing HIV-1 regimen. The primary efficacy endpoint was the adjusted mean decline in HIV-1 RNA from Day 1 to Day 8. Beyond Day 8 through Week 96, all patients received open-label RUKOBIA plus an investigator-selected OBT. In the non-randomized cohort, patients had no fully active and approved antiretroviral agent(s) available at screening and received open-label RUKOBIA twice daily plus OBT from Day 1 onward.	FDA Link	7/2

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23	INQOVI® (decitabine and cedazuridine) Tablets	Taiho Oncology, Inc.	Treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.	Cytidine deamina se	Priority Review, Orphan Drug designation	The safety and efficacy of INQOVI were evaluated in two multicenter, open-label, randomized, 2-cycle, 2-sequence crossover study trials that included patients with MDS or CMML. In both trials, patients received INQOVI (35 mg decitabine and 100 mg cedazuridine) orally in Cycle 1 and decitabine 20 mg/m2 intravenously in Cycle 2 or the reverse sequence. Both INQOVI and intravenous decitabine were administered once daily on Days 1 through 5 of the 28 day cycle. Starting with Cycle 3, all patients received INQOVI orally once daily on Days 1 through 5 of each 28-day cycle until disease progression or unacceptable toxicity. The efficacy was established on the basis of complete response (CR) as per the International Working Group (IWG) 2006 consensus criteria.	FDA Link	7/7
24	XEGLYZE (abametapir) Topical Preparations	Dr. Reddy's Laboratori es	The topical treatment of head lice infestation in patients 6 months of age and older	louse metallopr oteinase s	Standard	The safety and efficacy of XEGLYZE were established in two multi-center, randomized, double-blind, vehicle-controlled trials. Enrolled patients were 6 months of age and older with head lice infestation. All patients received a single application of either XEGLYZE or vehicle. For the evaluation of efficacy, the youngest patient from each household was considered to be the index patient of the household. Efficacy was assessed as the proportion of index patients who were treated with a single 10-minute application and were free of live lice at all follow-up visits on Days 1, 7, and 14.	FDA Link	7/24

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25	LAMPIT (nifurtimox) Tablets	Bayer HealthCare Pharmaceuticals, Inc.	The treatment of Chagas disease (American Trypanosomiasis), caused by Trypanosoma cruzi.	Nitroreductases; Glyceraldehyde-3-phosphate dehydrogenase, glycosomal	Priority Review, Orphan Drug designation	The safety and efficacy of LAMPIT were established in one randomized, double-blind, parallel-group, historically controlled trial in children with Chagas disease. Children less than 18 years of age with serologic evidence of T. cruzi infection and without Chagas disease-related cardiac or gastrointestinal symptoms were randomly assigned to receive LAMPIT three times a day for either 30 or 60 days and were followed for 1 year. Serological response to treatment was defined as ≥20% reduction in optical density measured by lysate and recombinant ELISA in subjects >8 months to <18 years or seroconversion to negative (defined as negative immunoglobulin G concentration in all patients) at 1-year post-treatment follow-up.	FDA Link	8/6
26	EVRYSDI™ (risdiplam) Oral preparations	Genentech, Inc.	The treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older.	MATE1 and MATE2-K transporters	Priority Review, Orphan Drug designation	The safety and efficacy of EVRYSDI were evaluated in two clinical trials.Trial 1 (Infantile-Onset SMA) was an open-label, multicenter trial in patients with Type 1 SMA. Patients in the higher-dosage cohort had their dosage adjusted to the recommended dosage of 0.2 mg/kg/day before 12 months of treatment, while patients in the low-dosage cohort did not. Efficacy assessment was based on the ability to sit without support for at least 5 seconds (as measured by Item 22 of the Bayley Scales of Infant and Toddler Development – Third Edition (BSID-III) gross motor scale). These results were compared to the natural history of untreated infantile-onset SMA.Trial 2 (Later-Onset SMA) was a randomized, multicenter, double-blinded, placebo-controlled trial in patients with SMA Type 2 or 3. Patients 2-25 years of age were randomized 2:1 to receive EVRYSDI at the recommended dosage or placebo. The primary efficacy endpoint analysis was the change from baseline in MFM32 total score at Month 12.	FDA Link	8/7
27	OLINVYK (oliceridine) Intravenous injection	Trevena, Inc.	An opioid agonist indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.	Mu-type opioid receptor	Standard	The efficacy and safety of OLINVYK were established in two randomized, double-blind, placebo and active (morphine) -controlled trials. Trials 1 and 2 evaluated OLINVYK for the treatment of moderate to severe post-operative pain. Patients in Trial 1 had undergone a bunionectomy and received either placebo, morphine, OLINVYK 0.1 mg, OLINVYK 0.35 mg, or OLINVYK 0.5 mg for 48 hours. Patients in Trial 2 had undergone abdominoplasty and received either placebo, morphine, OLINVYK 0.1 mg, OLINVYK 0.35 mg, or OLINVYK 0.5 mg for 24 hours. If the trial medication was inadequate, patients may have received rescue pain medication. The analgesic effect was measured using the Summed Pain Intensity Differences over 48 hours (SPID-48) or 24 hours (SPID-24), respectively. The SPID is calculated by multiplying the Pain Intensity Difference (calculated by subtracting the pain intensity at a particular timepoint from the pain intensity at baseline) scores at each post-baseline time point by the duration (in hours) since the preceding time point, and then summing the values, over 48 or 24 hours.	FDA Link	8/7

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
						28Trial 3 was an open-label safety evaluation of OLINVYK at various doses in medical and surgical patients.		
28	WINLEVI (clascoteron e) Topical Preparation - Cream	Cassiopea SpA	The topical treatment of acne vulgaris in patients 12 years of age and older.	Androge n receptor	Standard	The safety and efficacy of WINLEVI were established in 2 clinical trials. Both trials were randomized, double-blind, placebo-controlled clinical trials designed to evaluate WINLEVI in patients 9 years and older with facial acne vulgaris. Patients were randomized to receive either WINLEVI or vehicle cream twice daily to affected areas. Efficacy was assessed at Week 12 by the proportion of patients in each treatment group with at least a 2-point reduction in IGA compared to baseline and an IGA score of 0 (clear) or 1 (almost clear), absolute change and percent change from baseline in non-inflammatory and inflammatory lesions.	FDA Link	8/26
29	Detectnet (copper Cu 64 dotatate injection) Intravenous injection	RadioMedi x, Inc.	Use with positron emission tomography (PET) for localization of somatostatin receptor-positive neuroendocrine tumors (NETs) in adult patients.	SSTR2	Priority Review, Orphan Drug designation	Trial 1 was a single-center trial that enrolled patients with known or suspected neuroendocrine tumors (NETs) and healthy volunteers. PET imaging results were compared to a composite reference standard consisting of a single oncologist's blinded assessment of subject diagnosis based on available histopathology results, reports of conventional imaging (MRI, contrast CT, bone scintigraphy, F 18 fludeoxyglucose PET/CT, F 18 sodium fluoride PET/CT, In 111 pentetreotide SPECT/CT, Ga 68 dotatate (PET/CT) performed within 8 weeks prior to DETECTNET imaging, and clinical and laboratory data including chromogranin A and serotonin levels. DETECTNET images from each patient were interpreted as either positive or negative for NET by three independent readers who were blinded to clinical information and other imaging results. Trial 2 re-analyzed data from a published single-center trial that enrolled patients with a history of neuroendocrine tumors (NETs) and compared copper Cu 64 dotatate imaging to results from other imaging and biopsy.	FDA Link	9/3
30	GAVRETO™ (pralsetinib) Capsules	Blueprint Medicines Corporatio n	The treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.	RET	Priority Review; Orphan Drug designation	There was one multicenter, open-label, multi-cohort trial that provided data to evaluate the safety and the efficacy of GAVRETO in adult patients previously treated with systemic therapy and in treatment-naïve patients with advanced or metastatic RET fusion-positive cancer. Patients received GAVRETO orally once daily until unacceptable toxicity or disease progression. The major efficacy outcome measure for all cohorts was overall response rate and duration of response as determined by a blinded independent review committee according to RECIST v1.1. Safety assessment was done on all patients who received at least one dose of GAVRETO.	FDA Link	9/4

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
31	VEKLURY® (remdesivir) Intravenous injection	Gilead Sciences, Inc.	The treatment of coronavirus disease 2019 (COVID-19) requiring hospitalization	Replicase polyprotein 1ab	Fast Track Priority Review designations; Material Threat Medical Countermeasure Priority Review Voucher; EUA	The safety and efficacy of VEKLURY were established in three clinical trials.Trial 1 was a randomized, double-blind, placebo-controlled clinical trial of hospitalized adult patients with confirmed SARS-CoV-2 infection and mild, moderate, or severe COVID-19 which compared treatment with VEKLURY for 10 days with placebo. The primary clinical endpoint was time to recovery within 29 days after randomization. Recovery was defined as discharged from the hospital without limitations on activities, discharged from the hospital with limitations on activities and/or requiring home oxygen, or hospitalized but not requiring supplemental oxygen and no longer requiring ongoing medical care.Trial 2 was a randomized, open-label, multi-center clinical trial in hospitalized adult patients with confirmed SARS-CoV-2 infection, an SpO2 of ≤94% on room air, and radiological evidence of pneumonia which compared 5 days of VEKLURY treatment with 10 days of VEKLURY treatment. The primary endpoint was the clinical status on Day 14 assessed on a 7-point ordinal scale consisting of the following categories:1. death;2. hospitalized, receiving invasive mechanical ventilation or ECMO;3. hospitalized, receiving noninvasive ventilation or high-flow oxygen devices;4. hospitalized, requiring low-flow supplemental oxygen;5. hospitalized, not requiring supplemental oxygen but receiving ongoing medical care (related or not related to COVID-19);6. hospitalized, requiring neither supplemental oxygen nor ongoing medical care (other than that specified in the protocol for remdesivir administration); and7. not hospitalized.Trial 3 was a randomized, open-label. a multi-center clinical trial of hospitalized adult patients with confirmed SARS-CoV-2 infection, SpO2 >94% and radiological evidence of pneumonia. The trial compared treatment with VEKLURY for 5 days, treatment with VEKLURY for 10 days, and standard of care. The primary endpoint was the clinical status on Day 11 assessed on a 7-point ordinal scale as described in Trial 2.	FDA Link	10/22
32	ZOKINVY™ (lonafarnib) Capsules	Eiger BioPharmaceuticals, Inc.	A farnesyltransferase inhibitor indicated in patients aged 12 months and older with a body surface area of at least 0.39 m2 to reduce the risk of mortality associated with Hutchinson-Gilford progeria syndrome (HGPS). It is also indicated in this same population	Protein farnesyltransferase/geranylgeranyltransferase type-1 subunit alpha; Protein farnesyltransferase subunit beta	Priority Review, Orphan Drug designation	The safety and efficacy of ZOKINVY were evaluated in two clinical trials of patients with HGPS or Progeroid Laminopathy. Trial 1 was an open-label, single-arm trial where patients received ZOKINVY for 24 to 30 months. Trial 2 was an open-label, single-arm trial that consisted of two phases. In the first phase, Trial 2 enrolled patients from completed Trial 1 and they continued ZOKINVY with additional therapies for about 5 years. In the second phase of Trial 2, treatment naïve patients received ZOKINVY for up to three years. The retrospective survival analysis was based on the mortality data from treated patients and data from matched untreated patients in a separate natural history cohort.	FDA Link	11/20

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
			for the treatment of processing-deficient progeroid laminopathies that either involves a heterozygous LMNA mutation resulting in the accumulation of a progerin-like protein or homozygous/compound heterozygous mutations in ZMPSTE24					
33	IMCIVREE (setmelanotide) subcutaneous injection	RHYTHM Pharmaceuticals, Inc.	Indicated for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS)	Melanocortin receptor 4	Priority Review, Orphan Drug designation	The safety and efficacy of IMCIVREE were evaluated in two identical 1-year, open-label trials, each with an 8-week, double-blind withdrawal period. Patients were 6 years and older and had genetically confirmed or suspected POMC or PCSK1 deficiency obesity (Trial 1), or genetically confirmed or suspected LEPR deficiency obesity (Trial 2). Dose titration occurred over a 2 to 12-week period, followed by a 10-week, open-label treatment period. Patients who achieved at least a 5 kg weight loss (or at least 5% weight loss if baseline body weight was <100 kg) at the end of the open-label treatment period continued into a double-blind withdrawal period lasting 8 weeks, including 4 weeks of IMCIVREE followed by 4 weeks of placebo (investigators and patients were blinded to this sequence). Following the withdrawal sequence, patients re-initiated active treatment with IMCIVREE at the therapeutic dose for up to 32 weeks. The endpoint for both trials was achieving a ≥10% weight loss after 1 year of treatment with IMCIVREE.	FDA Link	11/25

Number	New Drug formulation	Sponsor	indication	Drug target	Regulatory special program	Unique clinical design	Details	Approve Date
34	Gallium Ga 68 PSMA-11 Intravenous injection	UCLA Nuclear Medicine, UCSF Nuclear Medicine	For positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in menwith prostate cancer:• with suspected metastasis who are candidates for initialdefinitive therapy.• with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level	Prostate-specific antigen	STANDARD	The safety and efficacy of Ga 68 PSMA-11 were evaluated in two prospective, open-label trials (Trial 1 and Trial 2) in men with prostate cancer.Trial 1 enrolled patients with biopsy-proven prostate cancer who were considered candidates for prostatectomy and pelvic lymph node dissection. Patients underwent Ga 68 PSMA-11 PET/CT imaging followed by the surgery. The images were read by three blinded independent readers and compared to histopathology obtained from dissected pelvic lymph nodes.Trial 2 enrolled patients with biochemical evidence of recurrent prostate cancer after definitive therapy defined by serum PSA of >0.2 ng/mL more than 6 weeks after prostatectomy or by an increase in serum PSA of at least 2 ng/mL above nadir after definitive radiotherapy. All patients received a single Ga 68 PSMA-11 PET/CT or PET/MR from mid-thigh to the skull base. The images were read by three blinded independent readers and compared to at least one of the following: histopathology, imaging (bone scintigraphy, CT, or MRI) acquired at baseline or within 12 months after Ga 68 PSMA-11 PET, or serial serum PSA.	FDA Link	12/1
35	ORLADEYO ™ (berotralstat) capsules	BioCryst Pharmaceuticals, Inc.	Indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older	Plasma kallikrein	Orphan Drug designation	The efficacy and safety of ORLADEYO were established in one randomized, double-blind, placebo-controlled trial. The trial evaluated ORLADEYO for the prevention of angioedema attacks in adult and adolescent patients with Type I or II hereditary angioedema who experienced at least two investigator-confirmed attacks in the 8 weeks of the run-in period. Patients were randomized into one of three parallel treatment arms (ORLADEYO 110 mg, ORLADEYO 150 mg, or placebo) and received assigned medication once daily for 24 weeks. All patients could use rescue medications for the treatment of breakthrough angioedema attacks. The primary efficacy endpoint was the reductions in the HAE attack rate relative to placebo during the 24-week treatment period.	FDA Link	12/4
36	KLISYRI (tirbanibulin) Topical Preparations	Athenex, Inc.	Indicated for the topical treatment of actinic keratosis of the face or scalp	Proto-oncogene tyrosine-protein kinase Src; Tubulin beta chain	STANDARD		FDA Link	12/14

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37	ORGOVYX (relugolix) Tablets	Myovant Sciences GmbH	A gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the treatment of adult patients with advanced prostate cancer	Gonadotropin-releasing hormone receptor	PRIORITY		FDA Link	12/18
38	GEMTESA (vibegron) Tablets	Urovant Sciences	The treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults	Beta-3 adrenergic receptor	STANDARD		FDA Link	12/23