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The CenterWatch Monthly

In This Issue

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Tips for Improving Sponsor Payments: Simple but Effective Measures

By James Miessler

Sites are often advised on things they can do to improve the payment process on their end, but sponsors can also take action to make sites' financial situations significantly less stressful, according to one sponsor representative.

Many sites operate with little financial bandwidth, says Christopher Chan, IGM Biosciences' vice president of financial planning and analysis, creating the potential for big problems when sites don't get payments from sponsors for months at a time.

This is supported by the Society for Clinical Research Sites' 2021 Landscape Survey, which found 60 percent of sites run on three months of operating cash or less, a fact that should impel sponsors to make payments as easy, flexible and timely as possible.

"I came to a 'eureka' moment when talking to a lot of sites. I went, 'you're kind of like someone living paycheck to paycheck.' Cashflow is apparently a very big issue," Chan said. "As a very naïve sponsor-side person, I had no idea until I heard it again and again."

Very frequently, sponsors have processes in place that make site payments akin to "sausage-making" before the money actually makes it into site coffers, he says. Payments may only be cleared after monitoring visits occur, not after patient visits, for instance, turning a net 30-day payment into a 100-day or longer affair. "That sounds extreme, but it's extremely common."

Chan offered the following tips for sponsors at this year's SCOPE Summit:

Payment Frequency: Make It Monthly

Sponsors should aim to provide quicker, more frequent payments by making them monthly, if they can swing it. While this will cost them more depending on the avenue they take for site payments, whether that's through a CRO, a third-party vendor or internally, the positive effect on investigators and sites could justify the higher costs and effort involved in doing this.

Most of the companies Chan has worked with employed a quarterly approach to site payments; the problem with this is that's quarterly according to their own systems, he said.

If a visit occurs at the beginning of a quarter but the data — along with the invoice — aren't submitted to the sponsor until the end of the quarter, the site has to wait for 90 days plus however long the sponsor's payment system takes to get paid for that visit, he said. "The site might not be paid for maybe six months, on an extreme, for an activity that happened 5.99 months ago."

see **Sponsor Payments** on page 4

Improvement Can Be as Important as Cure in Alzheimer's Trials, Association Argues

By Michele Sullivan

Meeting a final endpoint is not the only measure by which trial success should be judged, say several thought leaders in Alzheimer's disease (AD) research; regulators should also consider any improvement along the way to a cure as clinically meaningful to patients and a valid basis for approving a drug.

In a new think piece in *Alzheimer's and Dementia*, the Alzheimer's Association and a working group of hand-picked experts argue that a 25 to 30 percent slowing of cognitive decline — about what patients experience with antiamyloid antibody treatment — is enough to make a clinically meaningful difference in their lives.

"I think that all of us in this field — researchers, public stakeholders, regulatory people and third-party payers — need to take a step back and ask ourselves, what do we really expect from these treatments, especially with the clinical tools that we use now to measure effect," Ron Petersen, the paper's lead author, told *The CenterWatch Monthly*. "Our group came to the conclusion that this might be it. It's still meaningful. It's still important to patients. But

see **Alzheimer's Trials** on page 5

Regulatory Update

FDA Issues Final Guidance on Cannabis Clinical Research

The FDA has finalized guidance on trials of human drugs containing cannabis and cannabis-derived compounds, offering updated direction on federally authorized sources for cannabis and providing references to relevant quality considerations.

The National Institute on Drug Abuse's (NIDA) Drug Supply Program (DSP), which provides cannabis grown under contract by the University of Mississippi, was formerly the only domestic, federally legal source for cannabis containing more than 0.3 percent delta-9 THC for use in clinical research. But this has changed since the agency's 2020 draft guidance, and sponsors and investigators now have multiple sourcing options beyond the program.

According to the final guidance, researchers may now use non-NIDA DSP sources of cannabis that contain more than 0.3 percent delta-9 THC on a dry weight basis (a THC level that renders the cannabis a Schedule I controlled substance), as well as non-NIDA DSP sources for cannabis at or under the 0.3 percent threshold, so long as FDA deems the source(s) to be of adequate quality during its IND review. They may also still use the NIDA DSP for sourcing cannabis stronger than the 0.3 percent delta-9 THC threshold, the guidance says.

Access the final guidance here: https://bit.ly/3iUIvns.

FDA Guidance Allows Alternative Data Sources for External Control Arms

The FDA says trial sponsors and investigators may use patient-level data from other trials and/or real-world data (RWD) sources as an external control arm in a new draft guidance.

The guidance offers direction on design, analysis and bias considerations for trials that employ external control arms. Data sources may include medical claims, registry and electronic health record (EHR) data. It does not go into designing/analyzing natural history studies, the reliability and relevance of various RWD sources or the use of external control arms in traditional randomized trials.

Because these trials don't randomize their participants, it's important that the treatment and control arm groups are as similar as possible, the guidance notes, and a number of factors, including demographic characteristics/comorbidities, disease attributes, clinical observations, concomitant therapies, and start of follow-up for the investigational treatment, should be considered.

Before initiating a trial, "consider the likelihood that such a trial design would be able to distinguish the effect of a drug from other factors that impact the outcome of interest and meet regulatory requirements," the FDA says.

Addressing potential biases in these trials is critical and best done in the design phase, the guidance says, and protocols should be finalized prior to their conduct, including the selection of the external arm and analytic methodology, rather than choosing the external arm after a single-arm trial.

Sponsors should prespecify their plans for measuring and analyzing data on compounding factors and sources of bias, the FDA advises, and recognize that there are limitations to identifying these confounding factors.

The guidance also cautions that suitable data on suspected confounding factors may be missing for some participants or measured differently between the external control arm and treatment arm. Before deciding whether an externally controlled trial is suitable, sponsors should verify that important prognostic characteristics can be evaluated in the data sources that will be used.

Read the guidance here: https://bit.ly/3WTlkbo.

Draft Guidance Recommends Oncology Trials Use Wide Range of Doses

Oncology drug trials should investigate a wide range of doses in as widely varied a population as possible rather than immediately titrating patients up to the maximum tolerated dose (MTD), the FDA said in a new draft guidance.

Trials should identify any patient characteristics that might significantly affect pharmacokinetics. If there aren't enough patients, or a wide-enough variety of patients, sponsors can use simulated exposure metrics in these subpopulations.

In addition, adaptive trial designs can be employed to drive patients to one or more dosage arms as interim analyses provide safety and efficacy data.

Sponsors should also focus on low-grade AEs as well as more serious problems. Low-grade AEs, like mild-moderate diarrhea, "may still significantly affect a patient's ability to remain on the drug for extended periods," the agency says.

The FDA has asked for comments on the draft by March 19.

Read the draft guidance here: https://bit.ly/3XDVyZD.

see **Regulatory Update** on page 3

Regulatory Update

continued from page 2

FDA Provides Draft Guidance on Early Lyme Disease Drug Development

A new FDA draft guidance for sponsors developing drugs to treat early Lyme disease focuses on trial designs for treatment of erythema migrans, a rash that often appears as one of the first symptoms in the disease's early stages.

The guidance advises sponsors to conduct two adequate, well-controlled randomized double-blind trials that do not use placebos, but notes that in some cases, robust findings from a single trial supported by other independent clinical and/or nonclinical data may be sufficient for demonstrating effectiveness to the FDA.

Trials should enroll participants who have early localized (a single rash lesion) or early disseminated (multiple rash lesions) disease and have resided in or traveled to a Lyme disease-endemic area. Generally, patients with musculoskeletal, neurologic or cardiac manifestations of the disease should not be enrolled.

Trials also should not enroll patients with ongoing symptoms attributed to a history of Lyme disease or another tick-borne infection, such as babesiosis, ehrlichiosis or anaplasmosis, the agency advises.

The draft guidance does not touch on general issues in statistical analysis or trial design. It also doesn't discuss pharmacology/toxicology or clinical pharmacology for Lyme disease drugs in development, as considerations in these areas are similar to other anti-infective drugs, the FDA says.

Comments on the draft guidance are due by April 3.

Read the full draft guidance here: https://bit.ly/3wWLGhL.

FDA FY 2021 Postmarketing Report Shows Sponsor Compliance Lagging

Sponsors still are falling behind in their postmarket reporting, according to the FDA's yearly update on progress of postmarketing requirements/commitments.

Counting both new drug applications (NDA) and biologics license applications (BLA), only 79 percent of the 752 annual postmarket reports that were due to the FDA in 2021 met their deadlines; 13 percent were late and 9 percent went unsubmitted.

These figures are very close to fiscal year 2020 stats, which show 24 percent of total annual status reports were either late or completely unfiled by sponsors.

Of the 566 expected NDA annual status reports in fiscal 2021, 79 percent came in on time, 12 percent were late and 10 percent were not submitted by sponsors at all.

For the 186 BLA status reports the agency anticipated last fiscal year, 78 percent were on time, 15 percent came in late and 7 percent were not filed.

Read the full report here: https://bit.ly/3HRNJsD.

EMA Releases Pediatric Addendum to Venous Thromboembolism Trial Guidelines

The European Medicines Agency (EMA) has created an addendum to its current guidelines on trials of venous thromboembolism (VTE) treatments that is intended to help sponsors expand studies to pediatric populations.

Extrapolation of data from adult trials to pediatric indications can be problematic in VTE, the addendum indicates, due to young children's immature coagulation/fibrinolysis systems, especially in children age two years and younger.

Pediatric trials should include participants of different age ranges, when possible, but the addendum advises against the inclusion of newborns in trials due to concerns about central nervous system bleeding. Instead, the addendum suggests, trials including newborns should be conducted only after pediatric data from other trials are available.

Read the addendum here: https://bit.ly/3KdeonS.

EMA Seeks Comments on New Stakeholder Platform for Improving Trials

The EMA is requesting public comment on its new multi-stakeholder platform, Accelerating Clinical Trials (ACT) EU, for improving clinical trials within the trade bloc.

According to the agency, ACT EU is intended to serve as a forum for regular discussions on improving clinical research in the EU and "will encompass all aspects of clinical trials, including design, conduct, statistical analysis, proposal of revision of regulation(s), transparency of data and patient engagement."

ACT EU, which was kicked off in January 2022, is a joint effort among the EMA, the European Commission and Heads of Medicines Agencies, a group representing the regulatory authorities of countries in the European Economic Area.

"The creation of a common platform will encourage interactions between stakeholders at EU level, promoting a shared understanding and enabling concerted action to improve the clinical trials landscape," the EU said.

Following the public consultation period, there will be a kick-off meeting for the platform in the second quarter of 2023, EMA said.

Read the EMA's announcement here: https://bit.ly/3X280B6.

Sponsor Payments

continued from page 1

Sponsors who make sites invoice them on payments, essentially treating them like a vendor, should cease this practice immediately, in Chan's view. "It's a very painful and inefficient process. I guarantee you if that invoice comes and there's something the sponsor doesn't like, it goes back and forth for eight months until someone gets paid," he noted.

In addition, sponsors should think about getting rid of net 30, net 45 or net 60 requirements for certain payments. This is very doable, Chan said, simply by directing their accounting systems to include the relevant payments in the next payment run.

Payment Holdback: 'Just Skip It'

To Chan, the practice of payment holdbacks (withholding a percentage of a payment to serve as motivation, such as to complete study close-out activities) should be nixed by sponsors altogether. The negatives of holdbacks are far greater than their benefits, he said, adding that he's heard over and over from sites that this practice is highly frustrating.

The number of problematic sites in a trial is usually minimal, Chan said, the motivation is only moderately effective and the degree to which holdbacks upset sites is massive. "Just skip it," he advised. "Just don't do the holdback."

Doing away with this practice will have an immediate positive impact on sites and investigators as well as accountants and other sponsor-side staff that have to assist in tracking holdbacks on an ongoing basis, Chan said.

Advance Payments: Create a 'Slush Fund'

Payment delays can't be avoided completely and they will happen; sponsors often have to adhere to strict financial controls that contribute to bureaucracy, CROs add another level to these controls when they're used to handle site payments, and things will simply just go wrong sometimes.

Consider allowing advance payments, even if just selectively and occasionally. Sponsors could establish a "slush fund" that sites can draw from, Chan advised, a concept similar to how CROs pay sites on a sponsor's behalf.

"In a way, when you use a CRO [for site payments], you're already doing this," he said, "because the way that works is the CRO says, 'Send me a bunch of money, put it in this escrow thing and we'll send it out, and when we start going down toward zero, we'll ask you for another big chunk.'"

"You can do that by site. It's a lot more work to track and so forth, but it can be done."

Sites and sponsors can collaborate on an advance payment process that mitigates potential risks to the sponsor. Sites, for example, can track advances in their own systems and automatically refund any unused balance. Doing this and convincing sponsors the risk is minimal will make sponsors much more agreeable to advance payments, Chan said.

Payment Expectations: Make Them Clear

Being open and up-front on whether payments are by visit or procedure from the beginning can save sponsors and sites headaches and possibly far worse. Not being fully aligned on this can completely bomb a sponsor's standing with sites, as Chan has seen firsthand.

He worked with a sponsor that paid by procedure, not by visit, an unusual but doable approach, Chan said, on a six-site trial in Hong Kong. One visit in the protocol included two items: a physical exam costing about $100 and an expensive test to the tune of thousands of dollars. For one site, the sponsor determined it would only pay for the physical, not the test, as the test wasn't needed and thus wasn't conducted. It quickly became apparent, however, that the site's investigator expected to be paid for the test, a pricey scan, all the same.

"That investigator was livid," Chan said. "We tried to explain and the guy was still livid to the point where he said, 'I'm never working with your company ever again.'"

To make matters worse, the investigator was a key opinion leader in his field and friends with the other trial investigators. That single incident destroyed the sponsor's reputation with the sites. Was it worth not paying for the test, sticking hard to sponsor procedure and taking a huge hit with sites as a result? Chan said it's worth thinking about. "When you add all that up, it came to something like $50,000," he said. "Not insignificant for you and me, but is that worth the reputation hit?"

The CTA: To Include or Not?

To avoid such a situation, it's important that sponsors specify such details clearly in the clinical trial agreement (CTA) itself and specifically discuss payment expectations with sites as negotiations play out.

If you're reluctant to put these details in the CTA, at least have that conversation with investigators, a nonlegally binding approach that will help reduce miscommunication in the future. An email exchange discussing these details, for example, can be referred to later on.

Lastly, Chan recommended sponsors assemble site budgets in a more conducive manner to avoid disasters like the incident he shared.

"Maybe [that incident] would have been avoided if the sponsor understood that in many, many cases, the scan would not be required," he mused. "Then why put it in the study visit? Take it out and make it an invoiceable, meaning it will only be paid when it's done and specifically invoiced, like a patient expense, for example. Then you avoid this problem altogether."

Alzheimer's Trials

continued from page 1

we can't expect to have dramatic changes when we intervene for 18 months in a pathologic process that's been evolving over decades."

Regulatory Reality

The notion that a trial can be a regulatory success with very modest clinical effects — or even without them — illustrates the complexity of this concept, said Michael Irizarry, Eisai Neurology's senior vice president of clinical research, in an interview. Trials are designed to detect differences between treatments, he said. A drug succeeds when it passes this predetermined threshold.

Although the concepts of treatment difference and clinical benefit are measured differently, they are inextricably linked, often in confusing ways. For example, both Eisai's Leqembi (lecanemab) and Biogen's Aduhelm (aducanumab) passed the threshold of treatment difference, decreasing brain amyloid more than placebo. But their accelerated approvals were based on this biomarker, which the FDA says is "reasonably" predictive of clinically meaningful change, not on actual clinical impact.

A traditional approval, on the other hand, requires proof of clinical benefit. This merging of the two concepts — treatment difference and clinical benefit — is what Eisai is now going for in its bid for full approval of Leqembi, which has demonstrated a 27 percent slowing of decline.

Regulators need to understand what this difference means to patients in a very granular way, Petersen said.

"These drugs do have a modest impact on the clinical outcome, and what we're trying to say is, that may be good. That may be very positive and meaningful for patients. We're trying to [help regulators] think along the lines of what is the clinical metric that's going to move it from accelerated to full approval."

The 30 Percent Difference

Both Aduhelm and Leqembi have won accelerated approval from the FDA. Arguments over messy data persist, but in general, after 18 months of treatment, Aduhelm slowed decline by 30 percent and Leqembi by 27 percent. That works out to about half a point difference between the placebo and treated groups on the Clinical Dementia Rating Scale — sum of boxes (CDRS-sb), a measure of cognition and function.

While the relative differences expressed as percentages sound large and impressive, the absolute difference between the treatment groups is, Petersen admitted, quite modest.

Nevertheless, he and his co-authors contend that it's enough to delay progression from mild cognitive impairment to early AD, at best for a few months.

"On the CDR memory domain, a 0.5 rating means someone has inconsistent forgetfulness that's kind of a nuisance, but relatively benign. But at a 1, just half a point more, it's beginning to interfere with daily activities. One can no longer do what he formerly did because of memory issues."

A change in disease trajectory could buy a patient a few more months in a less-disabled state, the working group wrote. "It is reasonable and natural that such losses, at these early stages of mild illness, would be meaningfully felt by most patients, families, and care partners and that delaying such losses for several months, and potentially longer for a minority of patients treated over several years, would be of meaningful value."

A Dissenting Opinion

In addition to Petersen, the association's panel included its Chief Science Officer Maria Carrillo and six other experts, all either well-known AD trialists with ties to drug companies or drug company representatives. Knowing the players is important to understanding where this thought experiment is coming from, said Lon Schneider, MD, who directs the University of Southern California State of California Alzheimer's Disease Center.

"These are the Alzheimer's Association's handpicked experts," he said in an interview, adding that two panelists — J. Scott Andrews of Takeda and Brandy Matthews of Eli Lily — wrote the first paper claiming that change of this depth is a clinically meaningful outcome for patients and for drug trials.

Schneider took what he too called "a realistic stance," although his conclusions were much different than Petersen's. In essence, he said, the paper tries to portray these small changes in disease trajectory as much more important than they really are.

It's all about getting investigational drugs over the finish line, he said.

"What they're trying to do in this paper is cynical. It's spin and advertising and an attempt to generate enthusiasm" in the face of less-than-stellar study results. "If you don't like the result, move the goalpost, kick a field goal and declare victory," Schneider said.

The Confounder of Time

Current trial data for antiamyloid treatments don't just show us where patients end up after 12 or 18 months of treatment, the panelists wrote. They also suggested that progression could continue to slow with longer treatment. And if these interventions began at the very

see **Alzheimer's Trials** on page 6

Alzheimer's Trials

continued from page 5

earliest stages of disease, or even presymptomatically, even modest reductions in decline could accrue cumulative benefits over time.

"It is not practical to conduct AD randomized controlled trials (RCT) over one to two decades, where we may fully appreciate the impact of early intervention," they wrote. "As a result, perhaps our expectation of trials in the AD space needs to be modified to be more realistic with respect to the underlying pathophysiology and its clinical impact."

An antiamyloid treatment alone can't be expected to confer any remarkable improvements, they wrote.

"Just as we treat hypertension today with diuretics, beta blockers, calcium channel antagonists, angiotensin-receptor blockers, angiotensin-converting enzyme inhibitors … we will likely need multiple therapeutic interventions to address complex pathological and cognitive issues of aging," they wrote. "This argument is not meant to 'lower the bar' of expectations of AD RCTs; rather, it is meant to view them from a realistic perspective."

Discussion Continues

The argument isn't close to being settled, adds Howard Fillit, chief science officer of the Alzheimer's Drug Discovery Foundation.

"We just have to address this perception of whether delaying or slowing the rate of cognitive decline and lost function by 30 percent is meaningful," said Fillit. "The irony here is that this is a disease that robs people of their ability to think — the thing that most people value more than anything else. Here we now have a class of drugs that slows down this rate of decline in cognition and function and we're arguing about clinical meaningfulness."

Nevertheless, cognitive changes, which can't be measured with a blood test or an MRI, don't carry the same weight as other easily measured outcomes, Fillit said.

"If you show a tumor shrinking on an image, that's a wonderful thing. But having an 80-year-old being able to recognize their family over a year or so, that's not considered in the same class for some reason. It's a battle we've been fighting for a long time."

To read the AA article, click here: https://bit.ly/3IOF2AU.

Study Lead Opportunities

CenterWatch analyzes data in its drug intelligence database to provide advance notice of clinical trials expected to enter the next phase of clinical development soon. Contact information is provided for follow-up. **Sponsors/CROs:** to list an upcoming trial here, contact Leslie Ramsey, 703.538.7661, lramsey@wcgclinical.com.

Company name	Drug name	Indication
phase 1		
ADARx Pharmaceuticals	ADX-324	Hereditary angioedema
Alligator Bioscience Aptevo Therapeutics	ALG.APV-527	Solid tumors expressing the 5T4 antigen
AltruBio	ALTB-268	Ulcerative colitis
Awakn Life Sciences	(S)-ketamine	Alcohol use disorder
Bristol Myers Squibb	EXS4318	Immunology and inflammation indications
Century Therapeutics	CNTY-101	Relapsed/refractory CD19-positive B-cell lymphomas
Dyadic International	DYAI-100 COVID-19 recombinant protein receptor binding domain booster vaccine	COVID-19
Illuminare Biotechnologies	Illuminare-1	Fluorescent agent to provide visualization and delineation of critical nerves during surgery
Mersana Therapeutics	XMT-2056	HER2+ advanced/recurrent solid tumors including breast, gastric, colorectal and non-small cell lung cancers
Neuron23	NEU-723	Parkinson's disease
Oligomerix	OLX-07010	Alzheimer's disease and other neurodegenerative disorders
TechnoDerma Medicines	TDM-180935	Atopic dermatitis
Vaxxas	Needle-free inactivated seasonal influenza quadrivalent vaccine	Seasonal influenza
VistaGen Therapeutics	PH10 pherine nasal spray	Major depressive disorder
VITRAC Therapeutics	VIC-1911 and VIC-1911 plus sotorasib	KRAS G12C-mutant non-small cell lung cancer
phase 1/2		
Anaveon	ANV419	Advanced melanoma
Aptose Biosciences	Tuspetinib	Relapsed/refractory acute myeloid leukemia
Arrowhead Pharmaceuticals	ARO-MMP7	Idiopathic pulmonary fibrosis
Artios	ART0380 plus gemcitabine	Platinum-resistant ovarian cancer
Ashvattha Therapeutics	[18F]OP-801 imaging agent	Amyotrophic lateral sclerosis
Astria Therapeutics	STAR-0215	Hereditary angioedema

see **Study Lead Opportunities** on page 8

Study Lead Opportunities continued from page 7

Company name	Drug name	Indication
phase 1/2 continued		
C4 Therapeutics	CFT1946	BRAF V600 mutant solid tumors
Cytovation	CyPep-1	Advanced melanoma refractory to checkpoint inhibitors
Immix Biopharma	IMX-110 plus tislelizumab	Advanced solid tumors
Immunis	IMM01-STEM	Muscle atrophy associated with knee osteoarthritis
Marengo Therapeutics	STAR0602	PD-1 refractory advanced solid tumors
Qurient	Q702 plus pembrolizumab	Advanced solid tumors
REGENXBIO	RGX-202	Duchenne muscular dystrophy
phase 2		
AmMax	AMB-05X	Tenosynovial giant cell tumor
Daewoong Pharmaceutical	Bersiposocin (DWN12088)	Idiopathic pulmonary fibrosis
Eloxx Pharmaceuticals	ELX-02	Alport syndrome caused by nonsense mutations in the COL4 gene
First Wave BioPharma	Enhanced adrulipase formulation	Exocrine pancreatic insufficiency in patients with cystic fibrosis
FSD Pharma	FSD201	Chronic pain associated with idiopathic mast cell activation syndrome
Highlightll Pharmaceutical	TLL-018	Moderate-to-severe plaque psoriasis
Kura Oncology	Ziftomenib	NPM1-mutant relapsed/refractory acute myeloid leukemia
SOTIO	Nanrilkefusp alfa	Colorectal cancer
Tonix Pharmaceuticals	TNX-1900 (intranasal potentiated oxytocin)	Chronic migraine headaches
Vaxart	Oral bivalent norovirus vaccine	Norovirus
phase 2b		
Pulmatrix	PUR1900	Allergic bronchopulmonary aspergillosis in patients with asthma
phase 3		
Bayer	Asundexian (BAY2433334)	Prevention of stroke in patients with atrial fibrillation
Bayer	Asundexian (BAY2433334)	Non-cardioembolic ischemic stroke or high-risk transient ischemic attack
Daiichi Sankyo	Datopotamab deruxtecan plus pembrolizumab	Previously untreated advanced or metastatic non-squamous non-small cell lung cancer
GSK	Bepirovirsen	Chronic hepatitis B infection
Innovent Biologics	Picankibart (IBI112)	Moderate-to-severe plaque psoriasis
Teva Pharmaceuticals	TEV-44749 (subcutaneous long-acting injectable olanzapine formulation)	Schizophrenia

FDA Actions

The following is a sampling of FDA regulatory actions taken during the previous month, compiled from CenterWatch and third-party sources, including the FDA and company press releases. For more information on FDA approvals, visit centerwatch.com/fda-approved-drugs.

Company name	Drug name	Indication	FDA action
Accutar Biotechnology	AC0676	Relapsed/refractory B-cell malignancies	IND approved
Arugula Sciences	SIG002	Symptomatic osteoarthritis of the big toe	IND approved
Ascletis Pharma	ASC10	Respiratory syncytial virus	IND approved
Axcella Therapeutics	AXA1125	Long COVID fatigue	IND approved
BioAegis Therapeutics	Recombinant plasma gelsolin	Acute respiratory distress syndrome	IND approved
Centessa Pharmaceuticals	LB101	Solid tumors	IND approved
Deka Biosciences	DK210	EGFR+ advanced solid tumors	IND approved
Egret Therapeutics	EGT 101	Delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage	IND approved
Ellipses Pharma	EP0042	Acute myeloid leukemia	IND approved
Escient Pharmaceuticals	EP262	Mast cell mediated disorders	IND approved
Gracell Biotechnologies	GC012F	Relapsed/refractory multiple myeloma	IND approved
Hinova Pharmaceuticals	HP518	Metastatic castration-resistant prostate cancer	IND approved
HuidaGene Therapeutics	HG004	RPE65 mutation-associated inherited retinal dystrophies	IND approved
ImmPACT Bio	IMPT-314	Aggressive B-cell lymphoma	IND approved
Inmagene Biopharmaceuticals	IMG-008	Inflammatory diseases	IND approved
Mirati Therapeutics	MRTX1133	Solid tumors with KRASG12D	IND approved
Pharmazz	Sovateltide	Acute cerebral ischemic stroke	IND approved
Rise Therapeutics	R-3750	Ulcerative colitis	IND approved
TScan Therapeutics	T-Plex	Solid tumors	IND approved
TScan Therapeutics	TSC-204-A0201	Solid tumors	IND approved
TScan Therapeutics	TSC-204-C0702	Solid tumors	IND approved
Carina Biotech	CNA3103	Advanced colorectal cancer	Safe to Proceed letter
HistoSonics	Edison System	Primary renal tumors	IDE approved

see **FDA Actions** on page 10

FDA Actions continued from page 10

Company name	Drug name	Indication	FDA action
Varian	Cardiac radioablation	High-risk refractory ventricular tachycardia	IDE approved
GSK	Jemperli (dostarlimab-gxly)	Mismatch repair-deficient (dMMR) recurrent or advanced endometrial cancer	Full approval granted
GSK	Jesduvroq (daprodustat)	Anemia caused by chronic kidney disease in adults on dialysis	Approved
Eli Lilly	Jaypirca (pirtobrutinib)	Relapsed/refractory mantle cell lymphoma following at least two lines of systemic therapy, including a BTK inhibitor	Approved
Stemline Therapeutics	Orserdu (elacestrant)	ESR1 mutated, ER+, HER2- advanced or metastatic breast cancer	Approved
TheracosBio	Brenzavvy (bexagliflozin)	Type 2 diabetes	Approved
ALK	Odactra (house dust mite allergen extract) tablet for sublingual use	House dust mite-induced allergic rhinitis in patients age 12 through 17 years	Approved for expanded age indication
Pfizer	Cibinqo (abrocitinib)	Moderate-to-severe atopic dermatitis	Approved for expanded age indication
Merck	Keytruda (pembrolizumab)	Stage IB, II or IIIA non-small cell lung cancer	Approved for expanded indication
Takeda Pharmaceuticals	Takhzyro (lanadelumab-flyo)	Prevention of hereditary angioedema attacks in pediatric patients age two to less than 12 years	Approved for expanded indication
BeiGene	Brukinsa (zanubrutinib)	Chronic lymphocytic leukemia or small lymphocytic lymphoma	Approved for new indication
Gilead Sciences	Trodelvy (sacituzumab govitecan-hziy)	Pretreated patients with HR+/HER2- metastatic breast cancer	Approved for new indication
Regeneron Pharmaceuticals	Eylea (aflibercept) injection	Preterm infants with retinopathy of prematurity	Approved for new indication
Seagen	Tukysa (tucatinib) plus trastuzumab	Previously treated RAS wild-type, HER2-positive unresectable or metastatic colorectal cancer	Accelerated approval
Abbott	Proclaim XR spinal cord stimulation system	Painful diabetic peripheral neuropathy	Approved

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