Drugs that Received Breakthrough Therapy Designation (BTD) from the FDA's Center for Drug Evaluation and Research (CDER) Office of Neuroscience in 2024*

Drug Product	CDER Review Division	Indication	Orphan Drug Designation (ODD)?	Evidentiary Basis for BTD	BTD Date	Sponsor
PF614-MPAR *extended-release oxycodone prodrug plus trypsin inhibitor nafamostat*	Anesthesiology, Addiction Medicine, Pain Medicine	**Severe pain (with protection against abuse and oral overdose)**	N/A	Phase 1b trial in healthy volunteers using optimal Phase 1a dose (25 mg PF614 + 1 mg nafamostat) demonstrated oxycodone release at 1-2 simultaneous doses but reduced oxycodone release at 3 or more simultaneous dose units.[1]	1/23/24	Ensysce Biosciences
Latozinemab *progranulin agonist monoclonal antibody*	Neurology	**Frontotemporal dementia due to progranulin gene mutation (FTD-GRN)**	Yes	Phase 2 trial (n=28) showed sustained 2-fold increase in progranulin levels in plasma and CSF throughout 12-month analysis and a trend toward delay in disease progression.[2]	2/7/24	Alector Inc./GSK
CYB003 *deuterated psilocybin analog*	Psychiatry	**Adjunctive treatment of major depressive disorder (MDD)**	N/A	Phase 1/2a (n=34) showed statistically significant improvement on Montgomery-Asberg Depression Rating Scale (MADRS) at 3 weeks and incremental and sustained benefits at 6 weeks.[3]	3/7/24	Cybin Inc.
Lysergide d-tartrate *LSD*	Psychiatry	**Generalized anxiety disorder (GAD)**	N/A	Phase 2b trial (n=198) showed rapid, clinically meaningful, statistically significant, and sustained reductions on the Hamilton Anxiety rating scale.[4]	3/7/24	Mind Medicine Inc.
Diazoxide choline XR *ATP-sensitive potassium channel activator*	Neurology	**Prader-Willi Syndrome**	Yes	Phase 3 trial (n=114) showed statistically significant reduction in Hyperphagia Questionnaire scores in treated patients versus matched cohort from Natural History cohort (n=229).[5]	4/29/24	Soleno Therapeutics
Delpacibart etedesiran *antibody oligonucleotide conjugate*	Neurology	**Myotonic dystrophy type 1**	Yes	Phase 1/2 extension trial (n=37) showed continued improvement at one year across all endpoints versus Natural History data.[6]	5/8/24	Avidity Biosciences
Bexicaserin *5-HT2C superagonist*	Neurology	**Seizures associated with developmental and epileptic encephalopathies (DEEs)**	Yes**	Phase 1b/2a trial (n=52) showed 59.8% reduction in median countable motor seizures for bexicaserin versus 17.4% for placebo. [7]	7/1/24	Longboard Pharmaceuticals
Cytisinicline *plant-based alkaloid*	Psychiatry	**Nicotine e-cigarette (vaping) cessation**	N/A	Phase 2 trial (n=160) showed continuous, statistically significant e-cigarette abstinence versus placebo. [8]	7/31/24	Achieve Life Sciences
Edaravone and dexborneol *cryoprotection combination therapy*	Neurology	**Acute ischemic stroke**	N/A	Phase 3 trial (n=914) showed statistically significant improvement on modified Rankin Scale (mRS) for Neurologic Disability at 90 days. [9]	9/5/24	Simcere Pharmaceuticals Group
NTX-001 *fusogen nerve fusion technology and device kit*	Neurology	**Peripheral nerve injury repair**	Yes	Phase 2a trial (n=52) showed lower adverse events and statistically significant improvement in hand function and symptomatology versus standard of care. [10]	9/11/24	Neuraptive Therapeutics Inc.
ATX-101 bupivacaine within a biopolymer drug delivery system	Anesthesiology, Addiction Medicine, Pain Medicine	**Post-surgical pain following Total Knee Arthroplasty (TKA)**	N/A	Phase 2 dose-ranging trial (n=112) showed sustained, clinically meaningful post-surgical pain relief for up to 4 weeks versus the active comparator, bupivacaine. [11]	12/3/24	Allay Therapeutics
Zorevunersen *antisense oligonucleotide*	Neurology	**Dravet syndrome** *with confirmed mutation, not associated with gain-of-function, in the SCN1A gene*	Yes**	Phase 1/2a and open-label extension (OLE) trials showed tolerability, substantial and sustained reductions in seizures, and meaningful improvement on multiple measures of cognition and behavior. [12]	12/4/24	Stoke Therapeutics Inc.
Tolebrutinib *Bruton's tyrosine kinase (BTK) inhibitor*	Neurology	**Non-relapsing secondary progressive multiple sclerosis (nrSPMS)**	N/A	Phase 3 study (n=1,127) showed the time to onset of 6-month confirmed disability progression (CDP) was delayed by 31% versus placebo (p=0,0026) and 10% of patients had disability improvement. [13]	12/13/24	Sanofi

*List includes publicly announced BTDs identified by Parexel between January 1 and December 31, 2024. The list may be incomplete because the FDA does not publicly disclose BTDs granted for products that are not yet approved, and not all companies publicly announce the BTD status of their products; also, we may have missed an announcement. The FDA discloses aggregate data on BTDs for investigational drugs but does not identify individual agents. CDER's Office of Neuroscience (ON) consists of four new drug review divisions: The Division of Neurology I, the Division of Neurology II, the Division of Psychiatry, and the Division of Anesthesiology, Addiction Medicine, and Pain Medicine.

N/A: ODD does not apply because the disease or condition is not rare.

** Bexicaserin and Zorevunersen have ODD and Rare Pediatric Disease Designation for the treatment of seizures associated with developmental and epileptic encephalopathy (DEE), of which Dravet Syndrome is one type.

Footnotes for Evidentiary Basis of BTD: [1] PF614-MPAR: BTD Announcement and Study Results; [2] Latozinemab: BTD Announcement and Study Results; [3] CYB003: BTD Announcement and Study Results; [4] Lysergide d-tartrate: BTD Announcement and Study Results; [5] Diazoxide choline XR: BTD Announcement and Study Results; [6] Delpacibart etedesiran: BTD Announcement and Study Results; [7] Bexicaserin: BTD Announcement and Study Results; [8] Cytisinicline: BTD Announcement and Study Results; [9] Edaravone and dexborneol: BTD Announcement and Study Results; [10] NTX-001: BTD Announcement and Study Results.; [11] ATX-101: BTD Announcement and Study Results; [12] Zorevunersen: BTD Announcement and Study Results; [13] Tolebrutinib: BTD Announcement and Study Results. The evidentiary basis for BTD is not reported in standardized language in corporate press releases. We included links to the reporting of the primary efficacy studies referenced in the BTD announcements (when available). The FDA's criteria for BTD require "preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy."