

Unlucky 13

Top Clinical Trial Failures of 2018

Each drug candidate is listed alphabetically. Also shown is each drug's sponsor(s), the indication for which the drug failed, the type of drug, and a brief account of how the drug failed.

2 Axalimogene filolisbac

Advaxis
Cervical + head and neck cancer
Targeted Lm-based immunotherapy

A Phase I/II combination trial with AstraZeneca's Imfinzi® was halted in March after a patient death, then resumed in July after C-level overhaul. In November, Advaxis said it would halt enrollment in the combination trial to maximize the efficient use of clinical funding resources.

5 EG-1962 (nimodipine microparticles)

Edge Therapeutics
Aneurysmal subarachnoid hemorrhage
Bioabsorbable microparticle

Edge ended the Phase III NEWTON2 study after concluding EG-1962 was unlikely to meet the primary endpoint. Edge reviewed strategic alternatives, resulting in its planned reverse-merger with **PDS Biotechnology**, expected to close in Q1 2019.

8 Ingrezza® (valbenazine)

Neurocrine Biosciences
Tourette syndrome
Selective VMAT2 inhibitor

Neurocrine began 2019 assessing Ingrezza's future in Tourette syndrome after its third trial failure in that indication, missing the primary endpoint in the Phase IIb T-Force GOLD Study. Ingrezza generated an estimated \$409M in the treatment of tardive dyskinesia.

11 Olumacostat glasaretil

Dermira
Acne vulgaris
Topical sebum inhibitor

Dermira effectively scrapped olumacostat glasaretil after it failed to reduce lesion counts or show 2+ grade IGA improvement in two Phase III trials. The drug was once projected to generate \$250M in annual sales.

3 Azeliragon (TTP488)

vTv Therapeutics
Alzheimer's disease
RAGE inhibitor

Shares plunged 71% after vTv halted azeliragon studies following an initial readout failure in Part A of the Phase III STEADFAST study. However vTv identified a subpopulation (Alzheimer's patients with type 2 diabetes) showing statistically significant benefit.

6 Epacadostat (INCB024360)

Incyte
Unresectable or metastatic melanoma
IDO1 inhibitor

Incyte downsized its epacadostat clinical program after a combination with Merck & Co.'s Keytruda® (pembrolizumab) failed the Phase III ECHO-301/KEYNOTE-252 trial. Two pivotal lung cancer trials of the combo were converted to Phase II studies.

9 Keyzilen® (AM-101)

Auris Medical Holding
Acute inner ear tinnitus
NMDA receptor antagonist

Auris has been weighing Keyzilen's future since March 2018, when the drug missed its primary endpoint in the TACTT3 trial of significant Tinnitus Functional Score improvement vs. placebo—Keyzilen's second Phase III failure in 19 months.

12 Verubecestat (MK-8931)

Merck & Co.
Prodromal Alzheimer's disease
BACE1 inhibitor

Merck & Co. dropped verubecestat from its late-stage pipeline after the drug failed the Phase III APECS study in February 2018—the drug's second late-stage failure. The first came in February 2017 in the EPOCH study.

1 Atabecestat (JNJ-54861911)

Janssen (Johnson & Johnson)
Alzheimer's disease
BACE inhibitor

Janssen halted clinical development of Atabecestat, ending a Phase IIb/III trial and a Phase II European long-term safety study, after citing "serious" elevations of liver enzymes in some study participants who received the drug.

4 BI 409306

Boehringer Ingelheim
Alzheimer's disease
PDE9 inhibitor

Boehringer Ingelheim shifted BI 409306's development focus to ongoing schizophrenia studies after missing efficacy endpoints in two Phase II trials in patients with cognitive impairment and memory dysfunction in Alzheimer's and schizophrenia.

7 HTL0018318

Sosei Group and Allergan
Lewy body dementia
Muscarinic M1 receptor agonist

The companies said Phase II studies in Lewy body dementia and other dementias, including Alzheimer's, would be delayed at least 6 months. The companies cited the need to investigate an unexpected toxicology finding that occurred in a single animal study involving nonhuman primates.

10 MM-141 (istiratumab)

Merrimack Pharmaceuticals
Pancreatic cancer
Tetavalent monoclonal antibody

Merrimack scrapped MM-141 after missing primary and secondary endpoints in the Phase II CARRIE trial, assessing the drug plus nab-paclitaxel in patients with previously untreated metastatic pancreatic cancer and high serum levels of free insulin-like growth factor-1.

13 VR475 (nebulized budesonide)

Vectura Group
Asthma
Drug-device combo with jet nebulizer

Vectura ended VR475 development in November after it failed a Phase III trial in adults and adolescents with severe uncontrolled asthma. Vectura added VR475 to its pipeline in 2014 by acquiring **Activaero** for €130M (\$147.6M).