Review Article

Revolutionizing Treatments: Recent Advances in Novel Drug Approvals – 2024

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ABSTRACT

Novel drugs, also known as New Molecular Entities (NMEs), are compounds with active moieties previously unidentified or unapproved by the FDA. These innovative drugs offer new treatment options, often addressing rare or chronic conditions and improving healthcare outcomes and cost-efficiency. NMEs are distinct from existing treatments, including generic drugs, and usually include "me-too" compounds with unique properties or first-in-class drugs introducing new mechanisms of action. The drug approval process for NMEs includes several stages: pre-clinical studies, three phases of clinical trials, and a New Drug Application (NDA) review, followed by post-marketing assessments. This rigorous process ensures the safety and efficacy of novel drugs. In cancer treatment, NMEs have driven advancements in gene therapy, immunotherapy, targeted therapy, advanced radiation therapy, and minimally invasive surgery, transforming patient outcomes. Despite the benefits, developing novel drugs is challenging due to high costs, complex disease mechanisms, and limitations in modeling. For rare diseases, incentives like the Orphan Drug Act encourage drug development, enabling treatment options for otherwise neglected conditions. Recent approvals include drugs for bladder cancer, pediatric glioma, WHIM syndrome, and Alzheimer's disease, highlighting their potential to address diverse health needs. Novel drugs significantly impact healthcare by advancing treatment possibilities, improving patient productivity, and enhancing quality of life, particularly for those with previously limited options. In 2024, multiple novel drugs were FDA-approved to address various conditions, including cancer, hypertension, Duchenne muscular dystrophy, and Alzheimer's disease. Key treatments include etanercept for pulmonary hypertension, donanemab for Alzheimer's, and pegulicianine as a cancer-detecting imaging agent, showcasing advances in targeted and innovative therapies.

Keywords: New Molecular Entities, New Drug Application, Food and Drug Administration.

INTRODUCTION

Newly synthesized drugs, often referred to as New Molecular Entities (NMEs), contain active moieties that have not been previously identified or approved by the FDA. These active moieties are the parts of a molecule or ion responsible for the physiological or pharmacological action of the drug. Novel drugs are distinct from those already approved and marketed in the U.S., providing new treatment options and addressing unmet medical needs. Many novel drugs are developed for rare or orphan diseases and chronic conditions, offering significant therapeutic and economic benefits by reducing healthcare costs and improving patient productivity.[1]

Definition and Distinction of Novel Drugs

A Novel Drug, or NME, is an active compound or molecule not previously approved by regulatory authorities such as the FDA or EMA. This distinguishes them from previously approved drugs for new conditions or generic drugs produced by different companies. NMEs include "me-too" compounds, which utilize the same mechanism of action as previously approved drugs but are still considered novel due to their unique pharmacological properties. First-in-class drugs, introducing new mechanisms of action, typically make up 20-40% of new approvals. Novel Drug Delivery Systems (NDDS) encompass innovative approaches for transporting pharmaceutical compounds in the body to achieve therapeutic effects safely and effectively.

The Novel Drug Approval Process

The drug approval process involves several rigorous phases to ensure safety and efficacy:

1. **Pre-clinical and IND Application**: Laboratory and animal studies to gather preliminary efficacy, toxicity, and pharmacokinetic information.
2. **Clinical Trials**: Conducted in three phases:
    - **Phase 1**: Focuses on safety with 20-80 healthy volunteers over about one year.
    - **Phase 2**: Assesses effectiveness in 40-300 patient volunteers with a specific condition over roughly two years.
    - **Phase 3**: Involves several hundred to 3,000 patients to determine effectiveness and identify side effects, running for about three years.
3. **New Drug Application (NDA) Review**: The manufacturer requests FDA approval for US marketing.
4. **Post-marketing Risk Assessments**: Monitoring safety and efficacy after the drug is available to the public through Phase 4 studies.[2]

Impact of Novel Drugs on the Healthcare System

Novel drugs have a profound impact on the healthcare system by improving physical abilities and health outcomes, particularly for individuals with poor initial health. They play

a crucial role in advancing treatment options and enhancing overall health measures.

Innovations in Cancer Treatment

Recent advancements in cancer treatment highlight the transformative potential of novel drugs:

- **Gene Therapy**: Zolgensma and Luxturna, for spinal muscular atrophy and inherited retinal disease, respectively, use viral vectors to address genetic root causes.
- **Immunotherapy**: Checkpoint inhibitors like Keytruda and Opdivo, and CAR-T cell therapies such as Kymriah and Yescarta, boost the body's immune response against cancer.
- **Targeted Therapy**: PARP inhibitors like Lynparza and ALK inhibitors such as Alecensa target specific enzymes or genetic mutations in cancer cells.
- **Advanced Radiation Therapy**: Proton therapy and stereotactic radiosurgery (SRS) offer precise targeting of tumors with minimal damage to healthy tissue.
- **Minimally Invasive Surgery**: Robotic and laparoscopic techniques enable precise and less invasive tumor removal, reducing recovery times and complications.

Challenges in Developing Novel Drugs

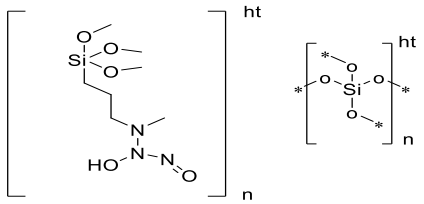
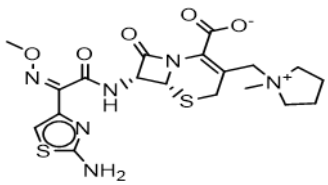
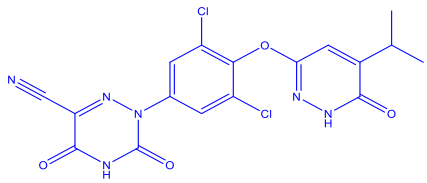
The development of novel drugs faces numerous challenges, including rising costs, limitations in modeling, and misunderstood disease mechanisms. Addressing these challenges is essential for more effective and financially sustainable drug discovery.

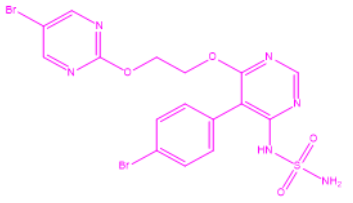
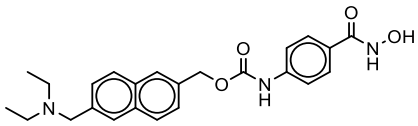
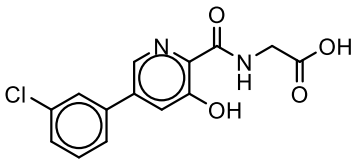
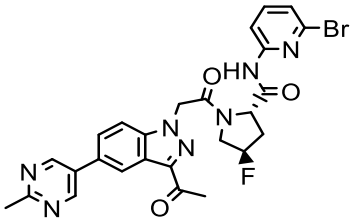
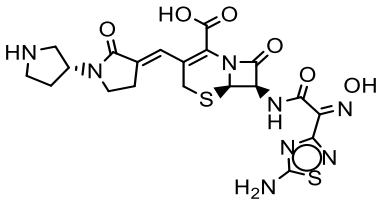
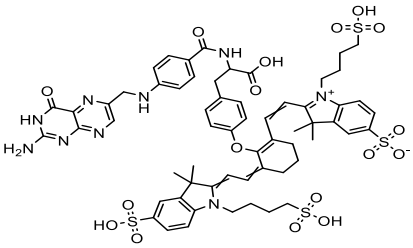
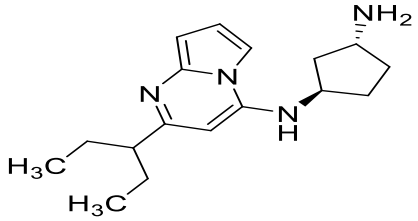
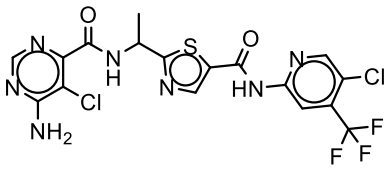
Treatment of Rare Diseases

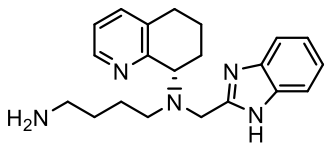
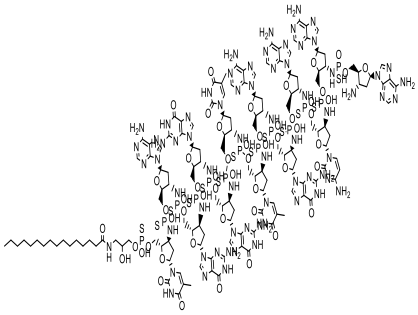
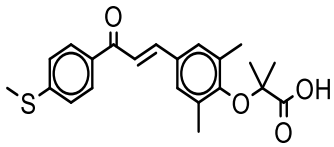
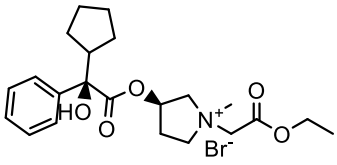
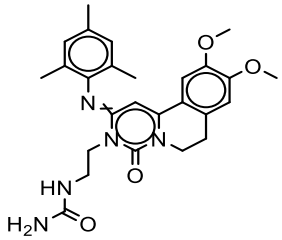
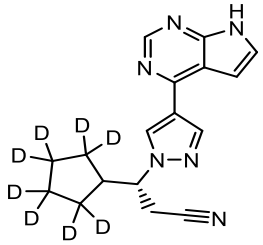
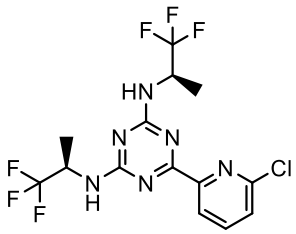
Rare diseases pose unique challenges due to their low prevalence and complexity. The Orphan Drug Act incentivizes drug development for rare diseases, making treatments more financially viable. Orphanet and the European Medicines Agency (EMA) contribute significantly to the database of orphan medicinal products in Europe. Table 1 shows the new approved drug list of 2024.

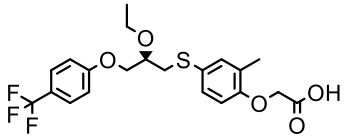
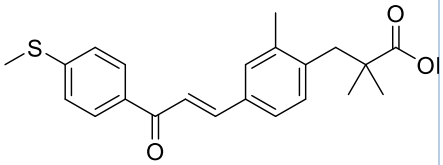
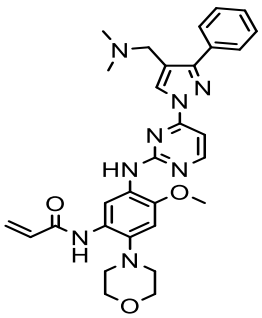
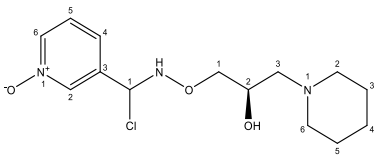
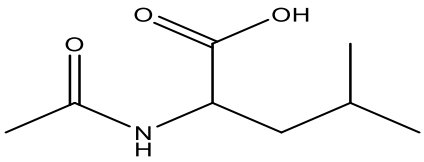
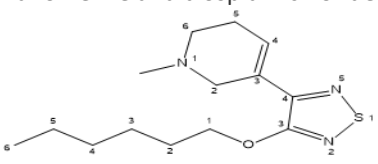
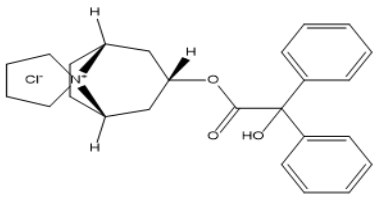
1. **Anktiva (nogapendekin alfa inbakicept-pmln)**: For bladder cancer.
2. **Ojemda (tovorafenib)**: For pediatric low-grade glioma.
3. **Xolremdi (mavorixafor)**: For WHIM syndrome.
4. **Imdelltra (tarlatamab-dlle)**: For extensive-stage small cell lung cancer.
5. **Rytelo (imetelstat)**: For myelodysplastic syndromes.
6. **Iqirvo (elafibranor)**: For primary biliary cholangitis.
7. **Sofdra (sofpironium)**: For primary axillary hyperhidrosis.
8. **Piasky (crovalimab-akkz)**: For paroxysmal nocturnal hemoglobinuria.
9. **Ohtuvayre (ensifentrine)**: For chronic obstructive pulmonary disease.
10. **Kisunla (donanemab-azbt)**: For Alzheimer's disease.[3]

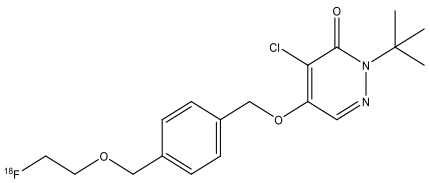
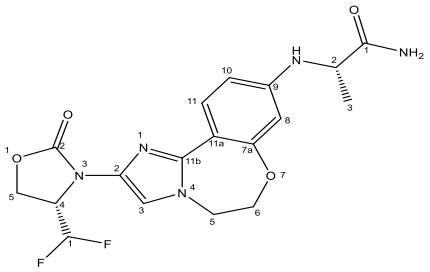
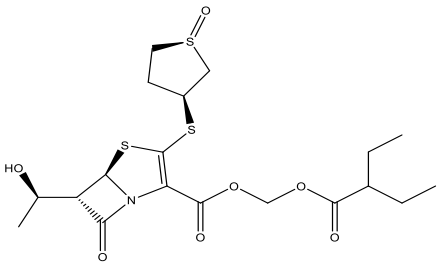
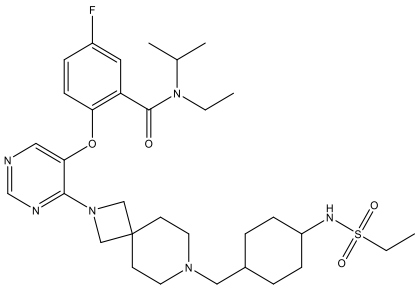
Table 1: The table is a list of CDER's novel drugs approvals for 2024

S No	Drug Name	Active Ingredient	Approval Date	on approval date FDA-approved use
1	Zelsuvmi	Berdazimer[4] 	1/5/2024	To treat molluscum contagiosum Berdazimer sodium is a nitric oxide releasing agent.
2	Exblifep	Cefepime, enmetazobactam[5] 	2/22/2024	Cefepime is commonly used to treat complicated urinary tract infections (UTIs), pneumonia, skin and soft tissue infections, and febrile neutropenia (in patients with weakened immune systems).
3	Rezdiffra	Resmetirom[6] 	3/14/2024	To treat non-cirrhotic non-alcoholic steatohepatitis (NASH) with moderate to advanced liver scarring, **resmetirom** is a thyroid hormone receptor beta (NR1A2) agonist. This medication works by selectively targeting the thyroid hormone receptor beta in the liver.

4	Tryvio	Aprocitentan[7] 	3/19/2024	To treat hypertension, aprocitentan is a receptor antagonist that targets both endothelin A and endothelin B receptors.
5	Duvyzat	Givinostat[8] 	3/21/2024	To treat Duchenne muscular dystrophy in individuals aged 6 years and older.
6	Vafseo	Vadadustat[9] 	3/27/2024	To treat anemia due to chronic kidney disease (CKD) in patients who have been on dialysis for at least 3 months. This medicine works by increasing erythropoietin (protein) to help the body make more red blood cells.
7	Voydeya	Danicopan[10] 	3/29/2024	To treat extravascular hemolysis with paroxysmal nocturnal hemoglobinuria.It is a complement inhibitor which reversibly binds to factor D to prevent alternative athway-mediated hemolysis and deposition of complement C3 proteins on red blood cells.
8	Zevtera	Ceftobiprole medocaril sodium[11] 	4/3/2024	To treat certain bloodstream infections, bacterial skin and associated tissue infections, and community-acquired bacterial pneumonia.
9	Lumisight	Pegulicianine[12] 	4/17/2024	To use as an optical imaging agent for the detection of cancerous tissue treatment for diseases caused by alpha-1 antitrypsin deficiency (AATD), such as chronic obstructive pulmonary disease (COPD) and liver disease.
10	Anktiva	Nogapendekin alfa inbakicept-pmln[13] 	4/22/2024	To treat bladder cancer Anktiva binds to receptors for the protein interleukin-15 (IL-15), which is found on certain types of immune cells. This may help the immune cells kill cancer cells better than BCG alone. Anktiva is a type of IL-15 receptor agonist and a type of immunotherapy.
11	Ojemda	Tovorafenib[14] 	4/23/2024	To treat relapsed or refractory pediatric low-grade glioma.

12	Xolremdi	Mavorixafor[15] 	4/26/2024	To treat WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis).
13	Rytelo	Imetelstat[16] 	6/6/2024	To treat low to intermediate-1 risk myelodysplastic syndromes. metelstat sodium works by blocking the activity of an enzyme called telomerase, which is found at high levels in cells that divide rapidly, including cancer cells. Blocking this enzyme keeps cancer cells from dividing and causes them to die.
14	Iqirvo	Elafibranor[17] 	6/10/2024	To treat primary biliary cholangitis in combination with ursodeoxycholic acid.
15	Sofdra	Sofpironium[18] 	6/18/2024	Treat primary axillary hyperhidrosis, a **topical anticholinergic agent**, such as **glycopyrronium tosylate**, is commonly used. Primary axillary hyperhidrosis is a condition characterized by excessive sweating in the underarm area, unrelated to other medical conditions. The topical anticholinergic agent works by inhibiting the activity of the sweat glands.
16	Ohtuvayre	Ensifentrine[19] 	6/26/2024	To treat chronic obstructive pulmonary disease (COPD), **ensifentrine** is an investigational dual inhibitor that targets enzymes involved in regulating airway inflammation and constriction.
17	Leqselvi	Deuruxolitinib[20] 	7/25/2024	To treat chronic obstructive pulmonary disease (COPD), **ensifentrine** is an investigational dual inhibitor that targets enzymes involved in regulating airway inflammation and constriction. To treat severe alopecia areata, **janus kinase (JAK) inhibitors**, specifically targeting **JAK1** and **JAK2**, are being developed for their immunomodulatory effects.
18	Voranigo	Vorasidenib[21] 	8/6/2024	To treat Grade 2 astrocytoma or oligodendroglioma.

19	Livdelzi	Seladelpar[22] 	8/14/2024	To treat primary biliary cholangitis (PBC)
20	Niktimvo	Axatilimab-csfr[23] 	8/14/2024	To treat chronic graft-versus-host disease (cGVHD).
21	Lazcluze	Lazertinib[24] 	8/19/2024	Treat non-small cell lung cancer (NSCLC), lazertinib works by blocking the activity of abnormal epidermal growth factor receptor (EGFR) proteins that signal cancer cells to divide. In many cases of NSCLC, mutations in the EGFR gene lead to the production of abnormal proteins that promote uncontrolled cell growth.
22	Miplyffa	Arimoclomol[25] 	9/20/2024	To treat Niemann-Pick disease type C (NPC), **arimoclomol** has been investigated as a potential therapeutic option. Arimoclomol is a **small molecule** that works by stimulating the heat shock response, which enhances the cellular machinery responsible for protein folding and the clearance of misfolded proteins. In diseases like NPC, which involve defective lipid trafficking and accumulation of abnormal proteins, arimoclomol may help reduce the buildup of misfolded proteins, thus improving cellular function.
23	Aqneursa	Levacetylleucine[26] 	9/24/2024	To treat Niemann-Pick disease type C (NPC), **levacetylleucine** is believed to modulate neuronal excitability, potentially by affecting ion channels, particularly potassium or calcium channels. This modulation may help stabilize neuronal activity, reducing abnormal neuronal firing that contributes to neurological symptoms commonly seen in NPC, such as ataxia, balance disorders, and motor dysfunction.
24	Cobenfy	Xanomeline and trospium chloride[27]  	9/26/2024	To treat schizophrenia. Blocks muscarinic receptors in the peripheral nervous system (outside the brain)Prevents cholinergic side effects such as excessive sweating, nausea, vomiting, and gastrointestinal discomfort caused by xanomeline

25	Flyrcado	Flurpiridaz F 18[28] 	9/27/2024	A radioactive diagnostic drug to evaluate for myocardial ischemia and infraction.
26	Itovebi	Inavolisib[29] 	10/10/2024	To treat locally advanced or metastatic breast cancer. Navolisib works by blocking the activity of a protein called PI3K-alpha that signals cancer cells to multiply. It also helps break down mutant versions of this protein found in cancer cells. This may keep cancer cells from growing and may kill them. Inavolisib is a type of targeted therapy drug called an enzyme inhibitor.
27	Orlynvah	Sulopenem etzadroxil, probenecid[30] 	10/25/2024	To treat uncomplicated urinary tract infections (uUTI). Penem β-lactam antibiotic, effective against multidrug-resistant bacteria.Inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs).
28	Revuforj	Revumenib[31] 	11/15/2024	To treat relapsed or refractory acute leukemia Blocking the interaction between menin and the rearranged KMT2A protein helps slow or stop the growth of leukemia cells. Revumenib citrate is a type of targeted therapy called a menin inhibitor.

CONCLUSION

In conclusion, the development of New Molecular Entities (NMEs)[32] is a key advancement in the pharmaceutical industry, offering new treatments for diseases with limited therapeutic options. These novel drugs, with unique mechanisms of action, provide valuable solutions for patients, particularly those suffering from rare and chronic conditions. By addressing unmet medical needs, NMEs enhance patient outcomes and help reduce overall healthcare costs. Although the process of developing NMEs is complex and resource-intensive, regulatory incentives such as the Orphan Drug Act have encouraged research into rare diseases, ensuring that these conditions are not overlooked. Recent FDA approvals highlight the potential of NMEs, with new treatments emerging for cancers, Alzheimer's disease, and other conditions. These breakthroughs offer hope for more personalized and targeted therapies, improving quality of life and productivity for patients. As the field progresses, the impact of NMEs will continue to be felt, transforming medical care for individuals worldwide.

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