FDA Approved Drugs: 2015-2019

Stages of a Drug

1. **Pre-clinical research** - initial design, SAR, in vitro and animal testing, formulation, etc.
   - Once a company has a viable candidate, they file an Investigational New Drug (IND) application to the FDA where they must disclose the drug’s composition and manufacturing, and a plan for human trials

2. **Clinical Trials** - happen only after FDA reviews the IND to make sure they don’t place humans at an unreasonable risk of harm and that there is adequate informed consent
   - **Phase 1**: comprised of between 20-80 healthy volunteers; emphasis on safety, used to determine side effects, metabolism, and excretion; takes about 1 year
   - **Phase 2**: 100-300 patients; emphasis on effectiveness and safety; takes about 2 years
   - **Phase 3**: 1000-3000 patients; continues to study safety and effectiveness while also evaluating effect on different populations, dosages, and in combination with other drugs

3. **NDA Review** - can take up to two and a half years; after clinical trials drug sponsor formally asks for FDA approval by submitting New Drug Application (NDA). Includes all animal and human data, analyses of the data, how drug behaves, and manufacturing. The FDA then has 60 days to decide whether to file NDA for review. During review FDA will review all data, label, and facilities where the drug is manufactured before either approving or issuing a response letter

What Factors FDA Considers During Approval

1. Analysis of a drug’s target and available treatments
2. Evaluation of a drug’s benefits and risks shown during clinical trials
   - In cases where the disease is rare/multiple trials aren’t feasible, convincing evidence from one trial may be enough. Usually expect results from two well-designed clinical trials
3. How risks will be managed

Other Designations

- **Accelerated Approval** - applied to therapies treating serious/life-threatening conditions and provide added benefit over all available therapies. Useful if drug treats disease whose course is long/requires long time to measure its effect. Therefore you only need to demonstrate an effect on a “surrogate endpoint” that should predict clinical benefit, or endpoint that is earlier but may not be as robust as a standard endpoint. Usually requires drug’s sponsor to conduct post-marketing clinical trials (if fail to show benefit FDA can withdraw approval)
- **Fast Track Designation** - given to drugs based on promising animal/human data. Assigned to speed up process to review for drugs treating serious conditions and fill an unmet medical need
- **Breakthrough Therapy** - given to drugs intended to treat a serious condition where preliminary evidences demonstrates there is a substantial improvement over available therapy. Also eligible for Fast Track
- **Priority Review** - FDA aims to tact on an NDA within 6 months of filing compared to standard 10 months. Reserved for drugs that would significantly improve the treatment, diagnosis or prevention of serious conditions
- **First-in-Class** - indicator of innovative nature of a drug. Often mechanism of action different from other existing therapies
- **Orphan** - drugs that treat rare diseases that affect 200,000 or fewer Americans. Usually few or no drugs available to treat these conditions because of rarity

Statistics of Drugs Approved in the Last 5 Years

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<th>2018</th>
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*Information available in the new year
**Hepatitis C Drugs**

- **Cause**: Hepatitis C virus, transmitted to humans by transfusion of body fluids
- **Symptoms**: affects the liver to develop liver Cirrhosis and carcinoma
- **Population**: WHO declared 71 million individuals suffering with chronic Hepatitis C infections
- **Treatment**: often involves a combination of direct acting antivirals (protease inhibitors, NS5B polymerase inhibitors, and NS5A inhibitors), pegylated interferon α and ribavirin.

**Recent Approved HCV Drugs**

- **Daclatasvir** - 2015 (Daklinza®, BMS)
  - EC₅₀ = 0.83 nM
  - genotypes 1 and 3

- **Velpatasvir** - 2016 (Epclusa®, in combo with Sofosbuvir, Gilead), HCV
  - EC₅₀ = 0.002-0.13 nM

**Hepatitis C Virus Genome**

- Single stranded positive sense enveloped RNA virus
- 7 types of genotypes (G1, G1a, G1b, G2, G3, G4, G5, G6 and mixed or others)
- Comprised of structural (Core Protein (Capsid), E1, E2 and Frameshift protein) and nonstructural polyproteins (P7, NS2, NS3S, NS4A/NS4B and NS5A/NS5B)
- Structural proteins have the functions at viral entry period into the cell
- Non-structural proteins required for viral reproduction
- Main targets to date in drug development around HCV NS₃/₄A and NS₅A/₅B
- NS₃-NS₄A protein multifunctional role in affecting host cell pathways
- NS₅A is vital for viral assembly, for interacting with RNA, the development of lipid raft composites which help in viral replication
- NS₅B has RNA-dependant-RNA polymerase (RdRp) activity which is significant for post-translational amendments of α-helical transmembrane; also interacts with numerous cellular proteins to regulate replication

---

FDA Approved Drugs: 2015-2019

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Baran Group Meeting
12/14/19

Glecaprevir

1. LiOH
2. F, HATU, DIPEA

RCM
1. LiOH
2. F, HATU, DIPEA

Voxilaprevir - 2017
(Vosevi®, in combination with Sofosbuvir and Velpatasvir, Gilead)
NS3/4A, all genotypes, EC₅₀ = 0.2-6.6 nM

Gilead Process Route:

J. Med. Chem. 2019, 62, 7340

Other Anti-Virals: HIV

• Cause: Human immunodeficiency virus, transmitted to humans by transfusion of body fluids
• Symptoms: targets the immune system and weakens people’s defence against infections and some types of cancer; advanced stage of infections is acquired immunodeficiency syndrome (AIDS)
• Population: WHO declared 37.9 million individuals living with HIV (end 2018)
• Treatment: involves a combination of lifelong antiretroviral drugs
• 5 drug targets: 1) nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), integrase strand transfer inhibitors (INSTIs), protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) and entry inhibitors

Bictegravir - 2018
(Biktarvy®, active ingredients include emtricitabine and tenofovir alafenamide, Gilead)
HIV-1 INSTI
EC₅₀ = 2.4±0.4 nM

As an INSTI Bictegravir works by disabling integrase, an enzyme essential for allowing HIV DNA to be put into human DNA inside CD4 T cells

Initial Route:

Made in 4 steps (all one pot)

No info on d.r.
**Asymmetric Routes to I:**

1. MgBr₂, 40-50°C in MeCN, DCM

2. HOAc, H₂O

3. (+)-γ-lactamase

4. (−)-Vince Lactam

5. MeCO₂H

6. 1. Pd(Ph₃)₄, HOAc  
   2. Ac₂O, imidazole

7. enzymatic desymmetrization

8. 1. hv, O₂, thiourea, MeOH, rose bengal  
   2. AcCl, Et₃N

**Deprotection (not specified)**

1. mCPBA  
   Tol, 25-30°C

2. LiOH, H₂O, MeOH

3. MeMgBr

4. 2-MeTHF

5. Boc

6. not isolated

**Bictegravir**

**OPRD 2019, 23, 716**

**Other Anti-Virals: Cytomegalovirus (CMV)**

- **Cause:** Cytomegalovirus, a common herpes virus that can remain dormant in the body but can cause complications during pregnancy and if immune system is weakened; spread through bodily fluids
- **Symptoms:** usually asymptomatic, if occur: fever, night sweats, tiredness, sore throat, swollen glands, joint and muscle pain, low appetite and weight loss
- **Population:** Over half of adults by age 40 have been infected
- **Treatment:** only required for babies with signs of congenital CMV and those with weakened immune systems

**Letermovir - 2017**

(Prevyms®, Merck)

Infection prevention after bone marrow transplant; acts as a CMV DNA terminase complex inhibitor

**EC₅₀ = 0.7-6.1 nM**

**ee further enriched with crystallization with tartaric acid derivative – final 99.6% ee**

**OPRD 2019, 23, 716**

**OPRD 2016, 20, 1097**
Cystic Fibrosis Drugs

- **Cause:** genetic autosomal recessive disease; mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene which maintain salt and fluid balance inside cells
- **Symptoms:** median survival 37-40 years, progressive lung damage, malabsorption in the intestinal tract and pancreatic insufficiency
- **Population:** affects one in every 3500 infants in the US, estimated 75,000 cases worldwide
- **Treatment:** “corrector” drugs which facilitate transport of proteins to the cell surface and “potentiator” drugs that facilitate chloride trafficking at the cell surface by increasing the time the gate of the protein is open

**FDA Approved Drugs: 2015-2019**

1. **Lumacaftor** - 2015 (Orkambi®, in combo with ivacaftor, Vertex)
   - **CFTR corrector**

2. **Tezacaftor** - 2018 (Symdeko®, active ingredient in combo with Ivacaftor, Vertex)
   - **CFTR corrector**

3. **Elexacaftor** - 2019 (Trikafta®, in combo with ivacaftor and tezacaftor, Vertex)
   - **CFTR corrector**

**1st generation route:**

1. HCl, 91%
2. CDI, DBU
3. 1. LiAlH₄ 60-63 ºC
   2. Aq. HCl
4. 
5. 

**Asymmetric Route:**

1. MeBu₃NCl, NaOH, CHCl₃, DCM
2. HCl, 99%
3. Resolution Route:

**2nd generation route:**

1. MeBu₃NCl, NaOH, CHCl₃, DCM
2. 1. LiAlH₄ 60-63 ºC
   2. Aq. HCl
3. 
4. Resolution Route:

**Mechanism?**

**Resolution Route:**

1. MeBu₃NCl, NaOH, CHCl₃, DCM
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1. MeBu₃NCl, NaOH, CHCl₃, DCM
2. 1. LiAlH₄ 60-63 ºC
   2. Aq. HCl
3. Resolution Route:
Boron-Containing Drugs

Due to boron’s empty p orbital, it can coordinate to heteratoms such as oxygen and nitrogen and form reversible covalent bonds with proteins. This has culminated in the approval of new therapeutics that work by these covalent mechanism.

Multiple Myeloma

• **Cause:** Cancer in plasma cells
• **Symptoms:** uncontrolled proliferation of monoclonal plasma cells in the bone marrow leading to the production of abnormal proteins
• **Population:** 1% of all cancers worldwide, 5-year survival rate of 45% (2009-2010)
• **Treatment:** targeted therapy (proteasome inhibitors such as Bortezomib/carfilzomib or moncolonal antibody drugs), biological therapy (drugs such as thalidomide/lenalidomide/pomalidomide), chemo, corticosteroids, bone marrow transplant, and/or radiation therapy

Ixazomib is a prodrug that is immediately hydrolyzed in aqueous solution to the boronic acid and form reversible covalent bonds with proteins. This has culminated in the approval of new therapeutics that work by these covalent mechanism.

Overproduction of cytokines can trigger inflammation.

Urinary Tract Infections

• **Cause:** Many different bacteria
• **Symptoms:** dysuria, urgency and frequency of micturition, pyuria, and the presence of high numbers of bacteria in the urine (>105/ml)
• **Population:** 150 million people each year worldwide
• **Treatment:** antibiotics

Vaborbactam acts as a non-suicidal beta-lactamase inhibitor that protects Meropenem (the penem antibacterial drug component of Vabomere) from degradation by certain serine beta-lactamas.

**Ixzomib Citrate - 2015**

(Ninlaro, Takeda Pharmaceuticals)

Multiple myeloma

**Crisaborole - 2016**

(Euceris®, Pfizer)

Eczema phosphodiesterase 4 inhibitor

Crisaborole 1st medication to treat atopic dermatitis that has been FDA-approved in more than 10 years. Works by targeting phosphodiesterase 4 enzymes which control cytokine function. Overproduction of cytokines can trigger inflammation.

Atopic Dermatitis (Eczema)

• **Cause:** Unclear, though suggestions that immunological system is involved/ cutaneous β-adrenoreceptors; physical or emotional stress can exacerbate
• **Symptoms:** inflammation/skin irritation
• **Population:** 2-5% (in children and young adults ~10%, 2014, World Allergy Organization)
• **Treatment:** usually resolves spontaneously between ages 5-8 but it can persist into adulthood; topical hydrocortisone, corticosteroids, and oral antihistamines could all be prescribed

Crisaborole 1st medication to treat atopic dermatitis that has been FDA-approved in more than 10 years. Works by targeting phosphodiesterase 4 enzymes which control cytokine function. Overproduction of cytokines can trigger inflammation.
FDA Approved Drugs: 2015-2019

Baran Group Meeting 12/14/19

Lisa M. Barton

**Phosphorus-Containing Drugs**

- Many instances of approved drugs containing phosphorus.
- Most often act as prodrugs (For instance improves aqueous solubility/PK) and/or improve activity

**Chronic Hepatitis B**

- **Cause:** hepatitis B virus; passed from mother to child or contact with bodily fluids
- **Symptoms:** chronic if test positive for >6 months, many do not exhibit symptoms and can be diagnosed decades after their initial exposure. inflammation and damage of the liver or liver cancer

**Arterial Thrombosis**

- **Cause:** activated by turbulent blood flow in diseased vessels or the release of mediators from other circulating cells and damaged endothelial cells lining the vessel
- **Symptoms:** result in a life-threatening partial or complete blood clots that can cause angina, heart attacks, or strokes

**Prodrug activation**

- Aryloxy phosphoramide triesters (ProTide) effective prodrug strategy for the transport of prodrugs within the cell. Both the aryl group attached to the oxygen and the stereochemistry of the methyl on the amino group, and a bulky alkyl group on ester crucial for effective biological action

**Active Drug**

- Recombivax HB - Effective Vaccine to prevent contracting the virus; effective drug therapies that control/stop further liver damage for those already infected

**Cangrelor - 2015**

(Kengreal®, The Medicines Co.)

Anticoagulant

- Direct-acting P2Y12 platelet receptor inhibitor that blocks adenosine phosphate-induced platelet activation and aggregation. P2 receptors are GPCRs that are only found on platelets. Cangrelor acts as a antagonist to the receptor
- To prevent enzymatic/chemical hydrolysis of polyphosphate side chain methylene unit placed between terminal and 2nd phosphate and chlorination gives it a pKa close to ATP

**Cangrelor**

- P=0.5
- Cl
- HO
- Me
- S
- N
- HO
- Cl
- 1. PO(OEt)₂
- 2. AcOH, Fe
- 3. NaOH, MeI
- 4. NaOH, H₂O
- 1. POCl₃ DIMEA
- 2. HNO₃, AcOH 80%
- 1. NH₃, 85%
- 2. HCl, CH(OEt)₃
- 3. NaOH, MeI
- 4. aq. NaHCO₃
- 5. aq. NH₄OH
- 6. aq. NaHCO₃
- 7. NaOH, H₂O
- 8. HCl, CH(OEt)₃
- 9. NaOH, MeI
- 10. aq. NaHCO₃
- 11. aq. NH₄OH
- 12. aq. NaHCO₃
- 13. NaOH, H₂O
- 14. HCl, CH(OEt)₃
- 15. NaOH, MeI
- 16. aq. NaHCO₃
- 17. aq. NH₄OH
- 18. aq. NaHCO₃

**Tenofiv Alafenamide Fumarate**

- 1. simulated moving bed chromatography
- 2. fumaric acid, MeCN 83%
- 3. NaOH, MeI
- 4. NaOH, H₂O
- 5. H₂O, DMF
- 6. NaOH
- 7. H₂O
- 8. NaOH
- 9. H₂O
- 10. NaOH
- 11. H₂O
- 12. NaOH
- 13. H₂O
- 14. NaOH
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- 90. NaOH
- 91. H₂O
- 92. NaOH
- 93. H₂O
- 94. NaOH
- 95. H₂O
- 96. NaOH
- 97. H₂O
**ALK-positive Non-Small Cell Lung Cancer**

- **Cause:** ALK positive tumors have an inversion in chromosome 2 that results in a novel oncogene, EML4-ALK. 5% of NSCLC tumors have this mutation. Associated with light smoking history and younger age
- **Symptoms:** cough, difficulty breathing, spitting/coughing blood, chest pain, hoarseness, problems swallowing, and eventually death
- **Population:** 5% of non-small cell lung cancer (NSCLC) contain this oncogene
- **Treatment:** 1st in line treatment is alectinib followed by ceritinib

**Chronic Immune Thrombocytopenia**

- **Cause:** autoimmune disorder
- **Symptoms:** antiplatelet autoantibodies and specialized white blood cells destroy their blood platelets and can damage their megakaryocytes, decreasing platelet production. This then causes excessive bleeding/bruising
- **Population:** Rare, fewer than 200,000 US cases/year
- **Treatment:** in children usually resolves itself, in adults steroids, splenectomy, immune globulin

**Breast Cancer**

- **Population:** 12% women will develop breast cancer, those with inherited BRCA mutations 69-72% more likely to develop breast cancer
- **Treatment:** surgery, chemotherapy, or PARP inhibitors (Talazoparib falls in this class). PARP inhibitors target poly (ADP-ribose) polymerases as they are important enzymes in DNA damage repair. Therefore their inhibition causes more single strand breaks

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**FDA Approved Drugs: 2015-2019**

**Brigatinib** - 2017 (Alunbrig®, Takeda)

- ALK-positive non-small cell lung cancer kinase inhibitor

**Key insight from SAR:**

- Et/Pr both enhanced selectivity but reduced potency over Me
- Basic nitrogen critical for driving cell-based activity; 6 membered rings best
- H best; F less active, Me equipotent cellular activity but loss in enzymatic activity

**Process Route:**

1. H2N
2. K2PO4, Pd(OAc)2, Xantphos, DMF 120 °C
3. H2N
4. K2CO3, n-Bu4NHSO4, DMF, 65 °C
5. HCl, EtOH, DME 20 °C

**Original配方：**

- Talazoparib - 2018 (Talzenna®, Pfizer)
- Breast cancer with germ-line BRCA mutations
- Originally targeting scaffolds such as:
- Planned synthesis:
- Novel structure for further SAR

WO 2016065028 A1

(Note med chem route extremely similar except Pd C-P formation done on NO2 anisole)
**FDA Approved Drugs: 2015-2019**

**Med Chem Route:**

- **Talazoparib**
  - J. Med. Chem. 2016, 59, 335
  - Process Route:
    - DMF, LiHMDS
    - -5 to 0 ºC
    - MeO-N
    - 2-MeTHF, 72.5%
  - No conditions given
  - Shown Route: WO 2015069851 A1

- Rolapitant
  - (Varubi®
  - Chemo-induced nausea
  - Alternative Routes: US 7,049,320; US 2008003640; CN 107383008
  - Shown Route: WO 2010028232 A1

**Process Route:**

- **Talazoparib**
  - J. Med. Chem. 2016, 59, 335
  - Process Route:
    - DMF, LiHMDS
    - -5 to 0 ºC
    - MeO-N
    - 2-MeTHF, 72.5%
  - No conditions given
  - Shown Route: WO 2015069851 A1

**Alternative Routes:**

- Varubi was discontinued in 2018 due to serious hypersensitivity reactions including anaphylaxis and anaphylactic shock. This may be due to the fact that the rolapitant IV emulsion contains soybean oil though other P/NK_{1} inhibitors that don’t contain soybean oil but have been associated with similar reactions.
FDA Approved Drugs: 2015-2019

2015

- Ceftazidime-avibactam (Avycaz®, Forest Laboratories)
  - Antibiotic
  - Helps treat infections

- Edoxaban (Farydak®, Novartis)
  - Anticoagulant

- Panobinostat (Farydak®, Novartis)
  - Multiple myeloma

- Cangrelor (Kythera biopharmaceuticals)
  - Anticoagulant

- Lumacaftor (Orkambi®, Vertex)
  - Cystic fibrosis

- Isavuconazonium sulfate (Cresemba, Baird)
  - Antifungal

- Sonidegib (Viberzi®, Forest Laboratories)
  - Basal cell carcinoma

- Eluxadoline (Viberzi®, Forest Laboratories)
  - IBS

- Rolapitant (Varubi®, Taiho Oncology)
  - Chemo-induced nausea

- Alectinib (Alecensa®, Genentech/Roche)
  - ALK-positive lung cancer

2016

- Sacubitril and Valsartan (Entresto®, Novartis)
  - Heart failure

- Brexpiprazole (Rexulti®, Lundbeck/Otsuka)
  - Schizophrenia

- Cariprazine (Vraylar, Allergan/Gedeon Richter)
  - Schizophrenia

- Daclatasvir (Daklinza, BMS)
  - Hepatitis C

- Trifluridine and Tipiracil (Odomzo, Novartis)
  - Colon cancer

- Trisodiumediphosphate (Theravance)
  - Anticoagulant

- Rolipram (Cytosol Pharmaceuticals)
  - Cystic fibrosis

- Palbociclib (Ibrance®, Pfizer)
  - Metastatic breast cancer

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FDA Approved Drugs: 2015-2019

2015

**Sugammadex** (Bridion®, Merck)
Anesthesia reversal

**Lesinurad** (Zurampic®, AstraZeneca)
Hyperuricemia

**Osimertinib** (Tagrisso®, AstraZeneca)
EGFR T790M mutation-positive lung cancer

**Obeticholic acid** (Ocaliva®, Intercept Pharmaceuticals)
Primary biliary cholangitis

**Rucaparib** (Rubraca®, Clovis Oncology)
BRCA-positive ovarian cancer

**Fluciclovine F 18** (Axumin®, Blue Earth Diagnostics)
PET imaging agent

2016

**Trabectedin** (Yondelis®, PharmaMar/J&J)
Soft-tissue sarcoma

**Cisaborole** (Eucerin®, Pfizer)
Eczema

**Lifitegrast** (Xiidra®, Shire)
Dry eye

**Obeticholic acid** (Ocaliva®, Intercept Pharmaceuticals)
Primary biliary cholangitis

**Venetoclax** (Venclexax®, AbbVie)
Chronic lymphocytic leukemia

**Tenofvir Alafenamide Fumarate** (Vemlidy®, Gilead)
chronic hepatitis B

**Brivaracetam** (Briviact®, UCB)
Epilepsy

**Velpatasvir** (Epclusa®, in combo with Sofosbuvir, Gilead)
HCV

**Grazoprevir** (A) and **Elbasvir** (B) (Zepatier®, Merck)
HCV genotypes 1&4

**Obatoclax** (GDC-0156, Genentech)
Acute myeloid leukemia

**Non-Small Molecules**

- Pafit hemophilia A
- Tresiba
- Praxbind
- Kanuma
- Strensiq
- Portrazza
- Nucala
- RePATHA
- Darzalex

**Non-Small Molecules**

- Patiromer
- Cosentyx
- Natpara
- Unituxin
- Praluent

- Empliciti
- Praxbind
- Kanuma
- Strensiq
- Portrazza
- Nucala
- RePATHA
- Darzalex

**Pimavanserin** (Nuplazid®, Acadia Pharmaceuticals)
Parkinson's disease associated Psychosis

- Toceranib
- Defitelio
- Cingair
- Taltz
- Anthim
- Adlyxin
- Zinbryta
Bictegravir (Biktarvy®, active ingredients include emtricitabine and tenofovir alafenamide, Gilead) HIV

Lofexidine hydrochloride (Lucemyra®, US WorldMeds) Opioid withdrawal

Avatrombopag (Doptelet®, Dova Pharmaceuticals, developed by AkaRx) Low platelet count in people with chronic kidney disease

Tezacaftor (Symdeko®, active ingredient in combo with Ivacaftor, Vertex) Cystic fibrosis

Apatamidine (Erleada®, J&J) Prostate cancer

Fostamatinib (Tavalisse®, Rigel Pharmaceuticals) Chronic immune thrombocytopenia

Tecovirimat (TPOXX®, SigaTechnologies) Smallpox

Binimetinib + Encorafenib (Mektovi® and Braftovi®, Array BioPharma) Metastatic melanoma

Tafenoquine (Krintafel®, GSK) Malaria

Cannabidiol (Epidiolex®, GW Pharmaceuticals) Seizures associated with Lennox-Gastaut and Dravet syndrome

Lutetium-177 dotatate (Lutathera®, Novartis) cancerous neuroendocrine tumors

Tecovirimat (TPOXX®, SigaTechnologies) Smallpox

FDA Approved Drugs: 2015-2019
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Non-Small Molecule

- Givlaari
- Polivy
- Adakveo
- Skyrizi
- Reblozyl
- Evenity
- ExEm Foam
- Cablivi
- Scenesse
- Jeuveau
- Beovu
- Avsola
- Ga-68-DOTATOC

Small Molecule

- Polivy
- Skyrizi
- Evenity
- Cablivi
- Jeuveau
- Avsola
- Ga-68-DOTATOC

Examples:

- Triclabendazole (Egaten®, Novartis)
  - Fascioliasis
- Relebactam (Recarbrio®, in combo with imipenem and cilastatin, Merck)
  - UTI/Intraabdominal infection
- Methotrexate (RediTrex®, Cumberland Pharmaceuticals Inc.)
  - Rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, and psoriasis
- Cefiderocol (Fetroja®, Shionogi&Co.)
  - Complicated UTIs
- Tafamidis meglumine (Vyndaqel®, Pfizer)
  - Heart disease cause by transthyretin mediated amyloidosis