In 2019, the FDA’s Center for Drug Evaluation and Research (CDER) approved 48 novel drugs [https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2019], which was fewer than the all-time record of 62 NTD approvals in 2018, but it was still a fruitful year. Among these approved drugs, 39 were targeted drugs (Table 1), including 27 small molecules, 3 antibody-drug conjugates (ADCs), 1 RNA interference (RNAi) therapy, 1 antisense oligonucleotide, 4 monoclonal antibodies (mAbs), 1 recombinant fusion protein, and 2 synthetic peptide analogs. The targets included kinases, ion channels, exons, enzymes, and receptors. Oncology, which remains the most important drug discovery area, accounted for 23% (9/39) of the targeted drug approvals.

Small molecule drugs play an important role in fighting diseases. Although the development of small molecules has slowed slightly in recent years, the 27 small molecule targeted drugs approved in 2019 accounted for nearly 70% of the total number of approved targeted drugs. Small molecule drugs have the advantages of oral bioavailability, pharmacokinetics, drug delivery, production cost, etc., which facilitate the development of this class of drugs, and this comparative advantage will continue in the near future. In addition, small molecules may be used in conjunction with new types of therapies, such as antibody-drug conjugates (ADCs).

In 2019, there was an increase in the number of approved ADCs: polatuzumab vedotin-piiq (Polivy) for relapsed or refractory diffuse large B-cell lymphoma, enfortumab vedotin-ejfv (Padcev) for refractory bladder cancer and fam-trastuzumab deruxtecan-nixi (Enhertu) for metastatic breast cancer. ADCs comprise a monoclonal antibody and cytotoxic agents conjugated via a chemical linker. The specificity of mAbs allows the chemotherapy agents to be selectively delivered to targeted cancer cells, thereby reducing toxicity. Importantly, mAbs such as trastuzumab not only show specificity but also have anticancer effects. To date, seven ADCs have been approved by the FDA for clinical use, and over 100 ADCs are in clinical development.  

Two synthetic peptide analogs were approved this year, bremmelanotide and afamelanotide. Peptide-based therapy has been applied in various diseases, such as infectious diseases, allergic diseases, autoimmune diseases, sexual dysfunction, and fibrosis. Many efforts have been made to discover novel bioactive peptides. There is much potential for peptide-based therapy. Another surprising newly emerging field in 2019 was gene therapy. In 2019, two gene therapy products were approved—Givlaari (givosiran) from Alnylam Pharmaceuticals and Vyondys 53 (golodirsen) from Sarepta Therapeutics. Givlaari is an RNA interference (RNAi) therapeutic that targets aminolevulinic acid synthase 1 (ALAS1) to treat acute hepatic porphyria (AHP). This is the second RNAi therapy approved by the FDA; Onpattro (patisiran) was the first. Onpattro was also developed by Aplylam Pharmaceuticals and was approved by the FDA in 2018 to treat hereditary TTR-mediated amyloidosis. Both drugs use enhanced stabilization chemistry (ESC)-GalNAc conjugate technology. Vyondys 53 is an antisense oligonucleotide developed from Sarepta’s phosphorodiamidate morpholino oligomer (PMO) platform; it was approved to treat Duchenne muscular dystrophy (DMD) patients who have a confirmed mutation of the dystrophin gene that causes exon 53 skipping. In the future, more gene therapies currently under development are likely to be approved in the upcoming years, which would bring hope to individuals with severe, life-threatening diseases or rare diseases.

The FDA approved Brukinsa (zanubrutinib) capsules from BeiGene USA, Inc., for the treatment of adult patients with mantle cell lymphoma who received at least one prior therapy. Brukinsa is the first novel antitumor cancer drug developed by a Chinese company and approved by the FDA. It was granted Accelerated Approval, Breakthrough Therapy designation, and Orphan Drug designation. Unfortunately, BeiGene, Ltd., announced that the new drug application (NDA) for zanubrutinib for the treatment of patients with relapsed/refractory mantle cell lymphoma (MCL) was accepted by the National Medical Products Administration (NMPA) on 08/27/2018, but zanubrutinib has not yet been approved.

On 08/30/2018, the China Food and Drug Administration (CFDA) changed its name to the National Medical Products Administration (NMPA), which is administered by the State Administration for Market Regulation (SAMR). In 2019, the NMPA approved 51 new drugs. Herein, we only summarize the eight innovative targeted drugs approved by the Chinese pharmaceutical industry (Table 2), including five small molecules, one antibiotic, one synthetic peptide analog, and two mAbs.

Two cancer immunotherapy drugs that target PD-1 have been approved, camrelizumab from Jiangsu Hengrui Medicine Co. and tislelizumab from BeiGene. Camrelizumab and tislelizumab are humanized IgG4 anti-PD-1 monoclonal antibodies that block the binding of PD-1 to its ligands. The first PD-1 inhibitor to hit the market was pembrolizumab (Krytruda), which was approved by the FDA in 2014. Since, ten PD-1/PD-L1 cancer immunotherapy drugs have come on the market worldwide, four of which were developed by Chinese pharmaceutical companies; these drugs are camrelizumab, tislelizumab, and sintilimab developed by Innovent Biologics and Eli Lilly and toripalimab developed by Shanghai Junshi Bioscience Co., Ltd. Following the FDA approval of Brukinsa (zanubrutinib), tislelizumab was the first drug developed by BeiGene to be approved in China. These young Chinese pharmaceutical companies show great potential in drug discovery, especially for novel targets. As China is the world’s second-largest pharmaceutical market, we expect to see an increase in the number of novel drugs developed in China.

New classes of drugs developed using new technologies provide new treatment options and hope to patients with fatal diseases. For example, the cancer mortality rate in the US declined by 29% from 1991 to 2017. This success is partially due to targeted therapies such as the BRAF inhibitor Zelboraf (vemurafenib) and the anti-CTLA4 antibody Yervoy (ipilimumab). In addition, emerging innovative therapeutic approaches such as CAR-T cell
| No. | Brand name | Active ingredient | Approval date | Target/Activity | FDA-approved use on approval date* | Drug class | Company |
|-----|------------|-------------------|---------------|----------------|-----------------------------------|------------|---------|
| 1   | Egaten     | Triclabendazole   | 2/13/2019     | Microtubule/tubulin | To treat fascioliasis, a parasitic infestation caused by two species of flatworms or trematodes that mainly affect the liver, sometimes referred to as “liver flukes” | Small molecule | Novartis Inc. |
| 2   | Zulresso   | Brexanolone       | 3/19/2019     | GABA receptor | To treat postpartum depression (PPD) in adult women | Small molecule | Sage Therapeutics |
| 3   | Sunosi     | Solriamfetol      | 3/20/2019     | Dopamine and norepinephrine transporters | To treat excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea | Small molecule | Jazz Pharmaceuticals |
| 4   | Mayzent   | Siponimod        | 3/26/2019     | Sphingosine-1-phosphate (S1P) receptor | To treat adults with relapsing forms of multiple sclerosis | Small molecule | Novartis Inc. |
| 5   | Evenity    | Romosozumab-aqqg  | 4/9/2019      | Sclerostin | To treat osteoporosis in postmenopausal women at high risk of fracture | Monoclonal antibody (mAb) | Amgen |
| 6   | Balversa   | Erdafitinib       | 4/12/2019     | FGFR family | To treat adult patients with locally advanced or metastatic bladder cancer | Small molecule | Janssen Biotech |
| 7   | Skyrizi    | Risankizumab-rrzaa| 4/23/2019     | Interleukin-23 (IL-23) | To treat moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy | Monoclonal antibody (mAb) | AbbVie Inc. |
| 8   | Vyndaqel   | Tafamidis meglumine| 5/3/2019    | Selective transthyretin (TTR) stabilizer | To treat heart disease (cardiomyopathy) caused by transthyretin-mediated amyloidosis (ATTR-CM) in adults | Small molecule | FOLDRX Pharms |
| 9   | Pipamy     | Alpelsib          | 5/24/2019     | PI3Kα inhibitor | To treat breast cancer | Small molecule | Novartis Inc. |
| 10  | Polivy     | Polatuzumab vedotin-piq | 6/10/2019 | Anti-CD79b antibody-drug conjugate (ADC) | To treat adult patients with relapsed or refractory diffuse large B-cell lymphoma | Antibody-drug conjugate (ADC) | Genentech Inc. |
| 11  | Vyleesi    | Bremelanotide    | 6/21/2019     | Melanocortin 4 receptor agonist | To treat hypoxic sexual desire disorder in premenopausal women | Synthetic peptide analog | AMAG Pharmaceuticals |
| 12  | Xpovio     | Selinexor         | 7/3/2019      | Selective CRM1 inhibitor | To treat adult patients with relapsed or refractory multiple myeloma (RRMM) | Small molecule | Karyopharm Therapeutics Inc. |
| 13  | Recarbrio  | Imerpenem, cilastatin and relebactam | 7/16/2019 | Imerpenem: β-lactamase inhibitor (previously FDA-approved antibiotic) cilastatin: dehydropeptidase inhibitor (previously FDA-approved antibiotic) relebactam: new β-lactamase inhibitor | To treat complicated urinary tract and intra-abdominal infections | Small molecule | Merck & Co., Inc. |
| 14  | Nubeqa     | Darolutamide     | 7/30/2019     | Androgen receptor (AR) antagonist | To treat adult patients with nonmetastatic castration-resistant prostate cancer | Small molecule | Bayer Healthcare |
| 15  | Turalito   | Pexidartinib     | 8/2/2019      | Colony-stimulating factor 1 receptor (CSF1R) | To treat adult patients with symptomatic tenosynovial giant cell tumor | Small molecule | Daiichi Sankyo Inc. |
| 16  | Wakix      | Pitolisant       | 8/14/2019     | Histamine H3 receptor inverse agonist | To treat excessive daytime sleepiness (EDS) in adult patients with narcolepsy | Small molecule | Harmony Biosciences |
| 17  | Rozlytrek  | Entrectinib      | 8/15/2019     | pan-Trk, ROS1, and ALK inhibitor | To treat adult patients with metastatic, ROS1-positive non-small-cell lung cancer (NSCLC) | Small molecule | Genentech Inc. |
| 18  | Inrebic    | Fedratinib       | 8/16/2019     | JAK2 inhibitor | To treat adult patients with intermediate-2 or high-risk primary or secondary myelofibrosis | Small molecule | Impact Biomedicines, Inc. |
| 19  | Rinvoq     | Upadacitinib     | 8/16/2019     | Janus kinase 1 (JAK1) inhibitor | To treat adults with moderately to severely active rheumatoid arthritis | Small molecule | AbbVie Inc. |
| 20  | Xenleta    | Lefamulin        | 8/19/2019     | 50S bacterial ribosome | To treat adults with community-acquired bacterial pneumonia | Small molecule | Nabiriva Therapeutics |
| 21  | Nouriinz   | Istadefylline    | 8/27/2019     | Adenosine A2A receptor antagonist | To treat adult patients with Parkinson’s disease experiencing “off” episodes | Small molecule | Kyowa Kirin, Inc. |
| 22  | Ibsrela    | Tenapanor        | 9/12/2019     | Na+/H+ exchanger NHE3 inhibitor | To treat irritable bowel syndrome with constipation in adults | Small molecule | Ardeylix, Inc. |
| 23  | Aklief     | Trifarotene      | 10/4/2019     | Retinoic acid receptor (RAR) agonist | | Small molecule | Galderma R&D |
| No. | Brand name | Active ingredient | Approval date | Target/Activity | FDA-approved use on approval date* | Drug class | Company |
|-----|------------|-------------------|---------------|----------------|-----------------------------------|------------|---------|
| 24  | Beovu      | Brolucizumab-dbll  | 10/7/2019     | Vascular endothelial growth factor (VEGF) inhibitor | For the topical treatment of acne vulgaris in patients 9 years of age and older | Monoclonal antibody (mAb) | Novartis Pharmaceuticals Corporation |
| 25  | Scenesse   | Afamelanotide     | 10/8/2019     | Melanocortin 1 receptor | To treat wet age-related macular degeneration | Synthetic peptide analog | Clivunel Inc. |
| 26  | Reyvow     | Lasmiditan         | 10/11/2019    | 5-HT1F receptor agonist | To increase pain-free light exposure in adult patients with a history of phototoxic reactions (skin damage) from erythropoietic protoporphyria | Small molecule | Bi Lily |
| 27  | Trikafta   | Lasmiditan         | 10/21/2019    | Lasmiditan: new cystic fibrosis transmembrane conductance regulator (CFTR) modulator ivacaftor: CFTR potentiator tezacaftor: F508del CFTR corrector | For the acute treatment of migraine with or without aura in adults | Small molecule | Vertex Pharmaceuticals |
| 28  | Reblozyl   | Luspatercept-aamt  | 11/8/2019     | Luspatercept-aamt | To treat patients 12 years of age and older with the most common gene mutation that causes cystic fibrosis | Small molecule | Eli Lilly |
| 29  | Brukinsa   | Zanubrutinib       | 11/14/2019    | Zanubrutinib | To treat certain patients with mantle cell lymphoma, a form of blood cancer | Small molecule | BeGene USA Inc. |
| 30  | Adakveo    | Crizanizumab-tmca  | 11/15/2019    | Crizanizumab-tmca | To treat patients with painful complications of sickle cell disease | Monoclonal antibody (mAb) | Novartis Inc. |
| 31  | Givlaari   | Givosiran          | 11/20/2019    | Givosiran: Aminolevulinic acid synthase 1 (ALAS1) | To treat acute hepatic porphyria, a rare blood disorder | Gene therapy: RNA interference (RNAi) | Alnylam Pharmaceuticals |
| 32  | Xcopri     | Cenobamate         | 11/21/2019    | Cenobamate: Sodium channel blocker | To treat partial onset seizures | Small molecule | SK Life Science, Inc. |
| 33  | Oxbyta     | Voxelotor          | 11/25/2019    | Voxelotor: Sickle hemoglobin (HbS) polymerization inhibitor | To treat sickle cell disease | Small molecule | Oxbyta to Global Blood Therapeutics |
| 34  | Vyondys 53 | Golodirsen         | 12/12/2019    | Golodirsen: Exon 53 | To treat certain patients with Duchenne muscular dystrophy | Gene therapy: antisense oligonucleotide | Sarepta Therapeutics |
| 35  | Padev      | Enfortumab vedotin- efv | 12/18/2019 | Nectin-4 | To treat refractory bladder cancer | Antibody-drug conjugate (ADC) | Seattle Genetics |
| 36  | Caplyta    | Lumateperone tosylate | 12/20/2019 | 5-HT2A receptor antagonist | To treat schizophrenia | Small molecule | Intra-Cellular Therapies, Inc. |
| 37  | Dayvigo    | Lemborexant        | 12/20/2019    | Lemborexant: Dual antagonist of the orexin OX1 and OX2 receptors | To treat insomnia | Small molecule | Eisai Inc. |
| 38  | Enhertu    | Fam-trastuzumab deruxtecan-nxki | 12/20/2019 | Trastuzumab: epidermal growth factor receptor 2 (HER2) deruxtecan: DNA topoisomerase I inhibitor | To treat metastatic breast cancer | Antibody-drug conjugate (ADC) | AstraZeneca and Daiichi Sankyo Company, Limited |
| 39  | Ubrelvy    | Ubrogepant         | 12/23/2019    | Calcinon gene-related peptide receptor (CGRP) antagonist | For the acute treatment of migraine with or without aura in adults | Small molecule | Allergan USA, Inc. |
therapy for cancer and CRISPR-Cas9 gene editing could potentially make a difference for patients.

In 2020, Signal Transduction and Targeted Therapy aims to be the leading forum for research addressing unmet medical needs, including cancer, immune disorders, infectious diseases, such as SARS-CoV-2, diabetes, cardiovascular diseases, inflammation, central nervous system diseases, and other pathologies. We expect to publish papers on the discovery and development of new targets and therapeutic options that may have a significant impact on healthcare in the future.

## REFERENCES

1. Mullard, A. 2019 FDA drug approvals. Nat. Rev. Drug Discov. 19, 79–84 (2020).
2. Oudard, S. N. 2018 FDA drug approvals. Nat. Rev. Drug Discov. 18, 593–594 (2019).
3. Siegel, R. L., Miller, K. D., & Jemal, A. Cancer statistics, 2020. CA Cancer J. Clin. 70, 7–30 (2020).
4. Siegel, L., Miller, K. D., & Jemal, A. Cancer statistics, 2020. CA Cancer J. Clin. 70, 7–30 (2020).

## ADDITIONAL INFORMATION

### Correspondence

Wenjing Wang (wangwenjing@wchscu.cn) or Qiu Sun (sunqiu@wchscu.cn)

### Editorial

Make a difference for patients.

In 2020, Signal Transduction and Targeted Therapy aims to be the leading forum for research addressing unmet medical needs, including cancer, immune disorders, infectious diseases, such as SARS-CoV-2, diabetes, cardiovascular diseases, inflammation, central nervous system diseases, and other pathologies. We expect to publish papers on the discovery and development of new targets and therapeutic options that may have a significant impact on healthcare in the future.