SEYFARTH SHAW

The BioLoquitur Bulletin

Drugs Available in 2018 For Generic Competition

Drugs Available in 2018 for Generic Competition

Parithosh K. Tungaturthi, Ph.D., J.D.
Dean L. Fanelli, Ph.D., J.D.
Thomas A. Haag, Ph.D., J.D.
Jamaica P. Szeliga, J.D.

This publication provides a brief overview of selected New Chemical Entities (NCE) that were approved by the FDA in the year 2014. While not every NCE will be a target for NCE-1 litigation, the Dissection Guide offers information about the drug products, indications, and Orange Book patents.

Please feel free to contact the authors, Parithosh K. Tungaturthi, at ptungaturthi@seyfarth.com, Dean L. Fanelli at dfanelli@seyfarth.com, Thomas A. Haag at thaag@seyfarth.com, or Jamaica P. Szeliga at jszeliga@seyfarth.com with any questions or comments.

This material was compiled: March 2018.

Table of Contents

Our Practice

Seyfarth Shaw LLP's Intellectual Property ("IP") practice is a full-service partner that helps clients identify and secure their intellectual property rights, exploit them in the marketplace, and enforce or defend them anywhere they do business. We bring the full strength of the firm to bear by leveraging all groups to effectively and efficiently address our clients' problems. This allows us to offer clients more than just legal services — our nationwide team of practitioners offers a full spectrum of solutions for your intellectual property needs. Seyfarth Shaw's IP Solutions also embraces SeyfarthLean®, our fresh approach to thinking about and executing the delivery of legal services. This new way of delivering value provides maximum efficiency and predictability to our IP clients.

We offer complete support relating to pharmaceutical and biological drug matters. Our team is experienced in the full scope of IP issues related to pharmaceutical product development and commercialization, from the initial counseling and pre-suit analysis to litigation under the Hatch-Waxman Act. We also serve as appellate counsel to clients even when other law firms served as trial counsel. Recognizing that appeals in the Federal Courts usually terminate with the intermediate court of appeals, we work to ensure that a client's victory is preserved on appeal or a negative verdict is overturned. Furthermore, we can assist clients in appeals to the U.S. Supreme Court either as counsel of record or as amicus counsel. Our firm also has significant experience in handling International Trade Commission (ITC) actions.

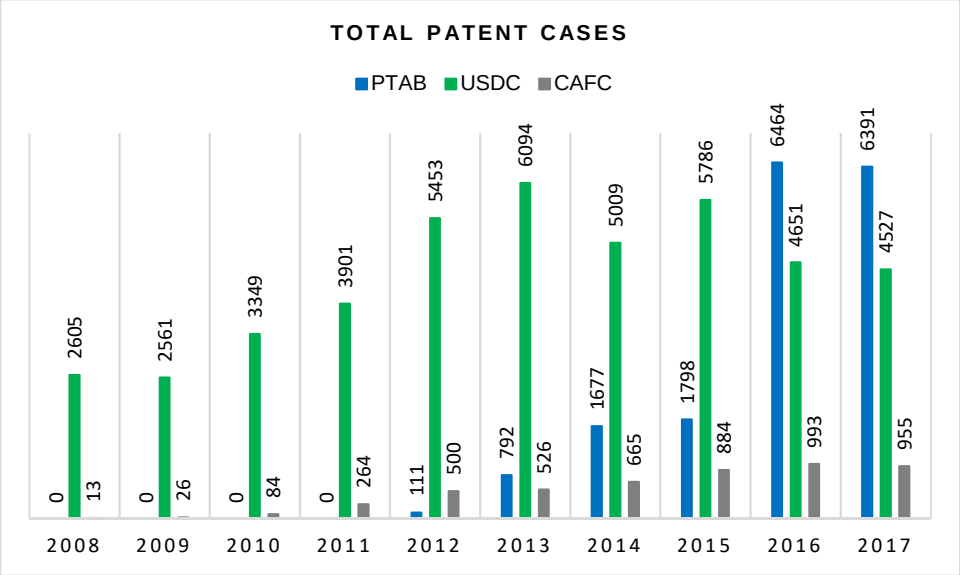
Our practice also includes experience in Food and Drug Law involving pharmaceuticals and medical devices. Seyfarth's Food and Drug Group represents clients whose businesses are regulated by the Food and Drug Administration (FDA) and the Federal Trade Commission (FTC). Our clients include companies that manufacture and distribute pharmaceuticals, bulk chemicals, vaccines, biologics, medical devices, and cosmetics, as well as food and dietary supplements. Our attorneys assist clients throughout the developmental, approval, production, and marketing stages of products to ensure that clients understand existing rules and regulations and the need to develop new strategies to address the regulatory environment. Our attorneys provide valuable counsel to FDA-regulated companies because we understand the regulatory and policy components of the FDA as well as the relationship between the FDA and Congress, and we know how to litigate matters concerning both the FDA and the FTC.

We further advise companies on the conduct of clinical studies on a national and international basis, on regulatory submissions and manufacturing as well as on FDA enforcement matters. Our attorneys have experience involving the labeling, marketing, and development of both pharmaceuticals and medical devices.

Seyfarth Shaw LLP represents a diverse roster of clients, from multi-national corporations to cutting-edge start-up companies. Whether we are acting as counselors, patent prosecutors or high-stakes litigators, Seyfarth is committed to obtaining our clients' desired results promptly and efficiently. We constantly

examine the strategy at each phase of the case until resolution. We also ensure that our cases and matters are staffed with the right team of lawyers and personnel, which offers clients both cost efficiency and a dedicated team backed by the strength and resources of one of the nation's premier law firms.

The number of new patent cases filed in the last ten years with the U.S. Patent Trial and Appeal Board (PTAB), the U.S. District Courts (USDC) and the Court of Appeals for the Federal Circuit (CAFC) are highlighted in the graph below. The District Court filings are consistent with the decreasing trend that can be seen during the last two to three years, the filings with the PTAB have risen significantly in the last 5 years, and the number of patent cases at the CAFC saw a steady increase from 2012 to 2016 and, more or less, remained stable over the last two years.



USDC patent case counts include cases addressing the infringement, validity, or enforceability of a U.S. patent that are pending in a U.S. district court or the Court of Federal Claims. This encompasses cases flagged with Nature of Suit ("NOS") 830 in the PACER system as well as other cases that are known to meet the above criteria. Transferred, consolidated, coordinated, or bifurcated actions may contribute to the number of cases counted.

PTAB cases include applications to the PTAB for *inter partes* reviews and post-grant reviews pursuant to 35 U.S.C. § 6(a)(4), as reported in the PTAB's Patent Review Processing System ("PRPS"). The term does not include proceedings conducted pursuant to 35 U.S.C. § 6(a)(1)-(3) such as appeals of adverse decisions of examiners, appeals of reexaminations, or derivation proceedings. Data obtained from Docket Navigator analytics.

Given the complex nature of IP litigation, whether at the District Court or PTAB, it is crucial to work with a patent litigation team that has deep knowledge of the relevant technology and the law at issue. Today's rapid technological advances demand not only a thorough understanding of the complex technology, but also a meticulous application of the intellectual property law to protect the technology.

Our legal team includes Ph.D.s that have expertise in organic chemistry, pharmacology, molecular biology, as well as drug synthesis, formulation and polymorphs. Our attorneys have represented some of the top innovator and generic drug companies in Hatch-Waxman litigation including in AIA proceedings, District Court trials and Federal Circuit appeals. When it comes to litigation or other complex projects, the Firm uses its award-winning and innovative SeyfarthLean® client service approach. Built upon years of experience in Lean Six Sigma process management, SeyfarthLean has a demonstrated success in improving communication, accountability, transparency and quality, while significantly reducing costs.

Hatch-Waxman Matters:

Our fully integrated approach to Hatch-Waxman litigation includes pre-suit investigations and opinions of counsel, Paragraph IV Certification/Notice Letter preparation, ANDA filings, trial, settlement, and appeal. We have represented both First to File clients as well as joint Abbreviated New Drug Application (ANDA) filers through joint defense arrangements.

From our deep bench, we are able to create legal teams of scientist-lawyers, transactional specialists, and experienced litigators, including those who served as law clerks at the Federal Circuit, which allows us to tailor our technology and legal strategy for each project and budget.

Our lawyers are recognized experts in the Hatch-Waxman Paragraph IV field and have been involved in some of the leading-edge Paragraph IV litigations.

The Firm has experience with the statutory and regulatory pathways to getting products to the market. Whether it is on the brand or generic side, in pharmaceutical or medical devices, Seyfarth has experience in all aspects of product management. Our experience includes the following areas:

- All aspects of pharmaceutical regulation, from inception to end-of-product life cycle management, product selection, including intellectual property review, freedom to operate, non-infringement and invalidity opinions, regulatory affairs counseling, size/shape/color opinions, and litigation management.
- Strategies relating to NDA, 505(b)(2) “Paper NDA,” ANDA applications, regulatory strategy and assistance in moving applications through the system.
- Drug repositioning, in legal issues related to new indications, new exclusivities, development of intellectual property estates to protect the repositioned drug, development of regulatory strategies to minimize competition, and counseling on legal strategies to maximize returns.
- Litigating exclusivity determinations relating to ANDA 180-day exclusivity decisions, NCE 5-year data exclusivity, NP/NDF 3-year exclusivity, and 7-year orphan drug exclusivity.
- Representing pharmaceutical and medical device clients with respect to licensing agreements, joint development agreements, manufacturing and supply contracts, fraud and abuse compliance,

group purchasing agreements, medical director agreements, and compliance with marketing standards.

- Regulatory strategies in medical device approvals, from counseling on strategies of 510(k) and PMA submissions, to humanitarian use exceptions, product recalls, product liability lawsuit defense, and corporate transactions.

Biologics and Biosimilars Matters:

The Biologics Price Competition and Innovation Act of 2009 (BPCIA) provides a legal framework for FDA approval of biosimilar and bio-interchangeable follow-on biologic products, as well as a paradigm for related patent litigation.

Our team of biotechnology attorneys routinely performs landscape searches and freedom to operate analyses with respect to target biologics for some of the world's top developers of Biosimilars. We understand both the value and potential threat represented not only by patents covering actual innovator biologics but also how to identify and handle the equally important patents related to biologic production, isolation, purification, storage, and administration.

Seyfarth lawyers have been involved in patent prosecution and litigation related to a variety of biotechnologies and have deep technical expertise in:

- Stem Cell Therapeutics and Screening Technologies
- Immuno-oncology and immunotherapies related to prophylactic and therapeutic cancer vaccines, CAR-T's and Checkpoint Blockades agonists
- Antibody technologies including fully human and humanized antibodies, antibody fusion proteins, phage display and bi-specific antibodies
- Nucleic Acid based drugs such as siRNA, miRNA, and mRNA
- Gene Therapies, e.g., AAV, Lentivrial and MVA vectors
- Epigenetic and gene editing technologies such as CRISPR/Cas9

We also keep abreast of the rapidly evolving biosimilars legal landscape and frequently blog and speak at industry conferences on this topic and BPCIA strategies.

Members of our team have served as General Counsel of biotechnology companies. As such, we understand the relevance of patent matters and weigh them in light of actual business strategies and if necessary address them through biosimilars patent litigation.

Seyfarth's Hatch-Waxman and Biosimilars Team

Seyfarth's Life Sciences team includes a multidisciplinary group of legal professionals with strong technical backgrounds in biology, biochemistry, organic chemistry, molecular biology, and pharmacology. Our team of experienced trial and appellate lawyers craft and execute comprehensive intellectual property strategies from initial drug development through trial and appeal.

Dean L. Fanelli, Ph.D. is a partner in the Intellectual Property Practice Group of Seyfarth Shaw LLP's Washington, D.C. office where he co-chairs the firm's chemical & life science patent team. Dr. Fanelli's practice focuses on the chemical, pharmaceutical, and biotechnology industries and his expertise lies in patent portfolio creation and management, counseling, technology transactions, due diligence, opinion work, including drafting novelty, freedom-to-operate, and invalidity opinions, and *inter partes* review and post grant review proceedings. Dr. Fanelli also focuses his practice on Paragraph IV litigation strategies, Hatch-Waxman litigation, and biosimilar market assessment and litigation strategy. Dr. Fanelli's expertise is in pharmaceutical and chemical related technologies including those in the fields of new chemical entities, pharmaceutical formulations, polymers, diagnostics, and medical devices. Dr. Fanelli also has significant experience with the interplay between patent and FDA laws under the Hatch-Waxman Act, and he regularly handles IP issues attendant to mergers, acquisitions, and financing for life sciences companies as well as Paragraph IV ANDA analyses and associated Hatch-Waxman Paragraph IV litigation.

Dr. Fanelli graduated from The George Washington University Law School. He received his Ph.D. in Organic Chemistry from Temple University and a B.S. in Chemistry from Villanova University.

Thomas A. Haag, Ph.D. is a partner in the Intellectual Property Practice Group of Seyfarth Shaw LLP's Washington, D.C. office where he co-chairs the firm's chemical & life science patent team. His practice focuses on pharmaceutical and biotechnology patent counseling, due diligence and licensing/transactional matters, as well as Hatch-Waxman litigation and patent opinion work. He has extensive experience strategically managing large patent portfolios, drafting and negotiating biomedical patent licenses, asset purchase agreements and joint-development agreements. Dr. Haag's technical expertise is in molecular biology related technologies including those in the fields of immuno-oncology,

cancer/infectious disease vaccines, nucleic acid-based therapeutics, stem-cell therapeutics, gene editing and therapy, epigenetics, transgenic plants, next generation sequencing (NGS), biologics and biosimilars.

Dr. Haag graduated from The George Washington University Law School with honors. He received his B.S. in Biology and Ph.D. in Molecular, Cell & Developmental Biology from UCLA.

Jamaica P. Szeliga is a partner in the Litigation Department of Seyfarth Shaw LLP's Washington, D.C. office. Ms. Szeliga's practice focuses primarily on intellectual property litigation relating to pharmaceutical, biotechnology, and chemical matters, particularly Paragraph IV litigation and litigation pursuant to the BPCIA. She also litigates patent disputes involving other technologies, including medical devices, mechanical inventions, communications, and high-tech products, and further has significant experience in design patent litigation. Ms. Szeliga's practice also extends to counseling on BPCIA strategies, patent prosecution, opinion drafting, and providing advice relating to intellectual property corporate transactions and trademark. Part of her practice is devoted to small entities, providing advice on ways to protect innovative ideas and procuring patents and trademarks for such entities.

Ms. Szeliga graduated *magna cum laude* from Harvard Law School, received her B.S. degree in Chemistry, with a minor in Biology, with distinction, from Stanford University, and clerked at the Court of Appeals for the Federal Circuit.

Vincent Smolczynski is an associate in the Intellectual Property Practice Group of Seyfarth Shaw LLP's Chicago office. He practices in the areas of complex civil litigation, patent litigation, and a variety of intellectual property matters. He also handles patent and trademark prosecution. Mr. Smolczynski's experience spans a wide range of technical areas, including pharmaceutical, chemical, biomedical devices, electronic devices, and business Methods. Mr. Smolczynski is registered to practice before the United States Patent and Trademark Office. Before joining Seyfarth Shaw, Mr. Smolczynski was a law clerk in the Intellectual Property Practice Group, assisting in various aspects of patent, trademark, and copyright matters. Mr. Smolczynski also served as a judicial extern for the Honorable Warren D. Wolfson in the Illinois Appellate Court, First District.

Mr. Smolczynski graduated *magna cum laude* from Chicago-Kent College of Law, and received his B.A., with honors, from The University of Delaware.

Maria L. Maebius is counsel in the Intellectual Property Practice Group of Seyfarth Shaw LLP's Washington, D.C. office. Ms. Maebius focuses on a wide variety of biotechnological and chemical inventions, including modified nucleic acids, sequencing Methods, stem cell differentiation, pharmaceutical delivery systems including transduced autologous cells, and immunological systems. Throughout her career as a patent attorney, she has worked on both sides of patents, including the preparation and prosecution of patent applications as well as reviewing and analyzing issued patents in developing litigation strategies or opinions relating thereto. She has experience in the management of patent portfolios of a variety of companies, including small start-ups, and medium to large biopharmaceutical companies. She has experience developing offensive and defensive patenting strategies, performing intellectual property audits to assess strengths and weakness of existing intellectual property, and preparing and prosecuting foreign and domestic patent applications. Additionally, she is experienced in preparing non-infringement and invalidity opinions and post-issuance patent proceedings, including reexaminations, reissue, and interference proceedings.

Ms. Maebius graduated from The George Washington University Law School, and received her B.S. degree in Biology from The Ohio State University.

Parithosh K. Tungaturthi, Ph.D. is a patent agent in the Intellectual Property Practice Group of Seyfarth Shaw LLP's Washington, D.C. office. Dr. Tungaturthi's practice focuses on the pharmaceutical and biotechnology industries and his expertise lies in the areas of patent portfolio creation and management, IP strategy development, patent landscape analysis, product lifecycle management, due diligence, and opinion work, including drafting novelty, freedom-to-operate, and invalidity opinions. Dr. Tungaturthi's practice also includes support of Paragraph IV, Hatch-Waxman litigation, and FDA Regulatory and Compliance matters. Dr. Tungaturthi has significant expertise in a broad range of disciplines including pharmaceuticals, active pharmaceutical ingredients, formulations, drug delivery, organic and inorganic chemistry, molecular biology, antibody engineering and therapeutics, cancer immunology, molecular diagnostics, genetic engineering, stem cell technology, vaccines, medical devices, plant breeding and plant biotechnology. He also has experience in nanotechnology, polymer chemistry, biomaterial, and biofuels.

Dr. Tungaturthi earned his J.D. from The University of Baltimore School of Law. He received his Ph.D. in Molecular Biology and Immunology from Thomas

Jefferson University and a B.S. in Microbiology, with a minor in Chemistry, from The Louisiana State University.

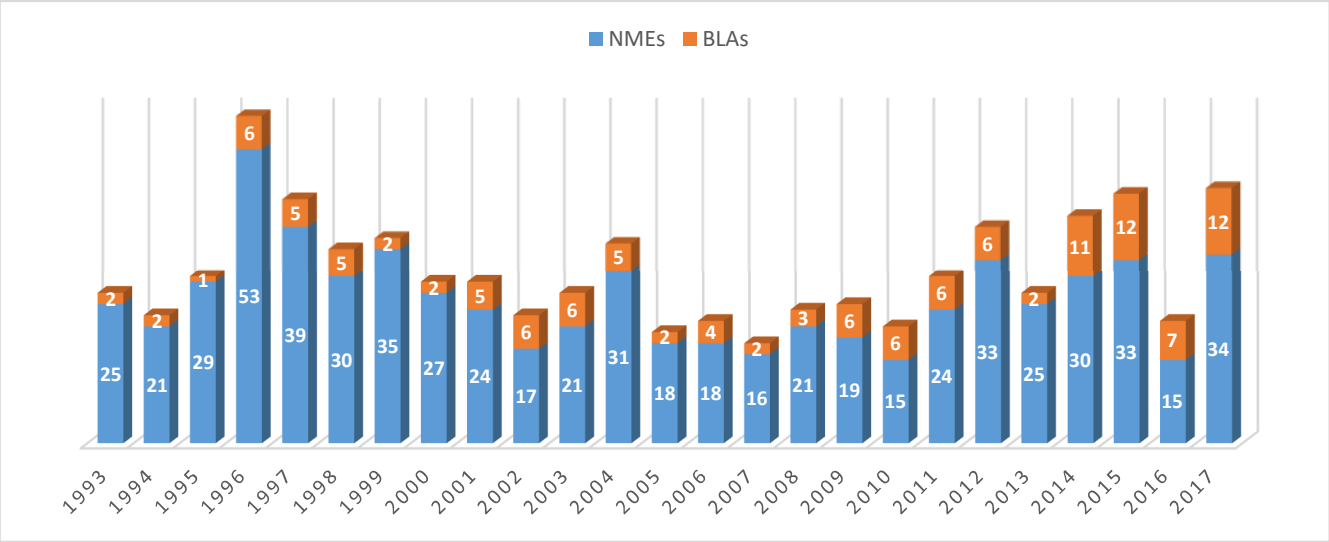
Robert Terzoli, Jr. is a member of the Intellectual Property Department of Seyfarth Shaw LLP's Washington, D.C. office. Mr. Terzoli has over five years of IP Experience, including conducting invalidity and freedom to operate searches, assisting with patent prosecution and trademark prosecution matters, working in-house as an intern and private equity company monetizing of IP assets.

Mr. Terzoli earned his J.D., with a concentration in Intellectual Property, from The Georgetown University Law Center and received his B.A. in History from UCLA.

Hatch-Waxman Act

The Hatch-Waxman Act was enacted in 1984 to address two main congressional goals: (1) to encourage innovation in pharmaceutical research and development; and (2) to help generic drugs reach the market more quickly. Through amendments to both the patent and the food and drug laws, the Act established several practices intended to provide brand-name firms with incentives to innovate while facilitating the marketing of generic pharmaceuticals.

Whether or not it was envisioned at the time, the use of generic drugs in the US has seen a tremendous increase since the enactment of the Act. From about 13% (of all prescriptions) in 1984, use of generic drugs grew to 50% by the late 1990s. As of 2016, generics accounted for 89% of prescriptions dispensed but only 26% of total medicine spending. Put another way, brand drugs are only 11% of prescriptions but are responsible for 74% of drug spending. Given the profit margin for generic drug manufacturers, it is not surprising to see ANDAs being filed at an incremental rate. A significant increase has been seen in the generic drug filings at, and consequently approvals by, the Food and Drug Administration (FDA). In 2017, the FDA set an all-time record for generic drug approvals and for more novel drugs than any year since 1996. A review of the number of drugs approved over the years is highlighted in the graph below.



Among other things, the Act included elaborate provisions governing the mechanisms through which a potential generic manufacturer may obtain marketing approval for a drug that has been patented by another party. The Act provides generic drug companies with certain procedures for challenging a new drug company's patent exclusivity for the Reference Listed Drug (RLD). For example, the generic drug company can file a Paragraph IV Certification in connection with the RLD.

New Drug Exclusivity

An exclusivity provides limited protection from new competition in the marketplace and precludes approval of certain ANDAs for prescribed periods of time. Certain exclusivities for qualifying brand name drugs and generic drugs were established in the Act. Another type of exclusivity for brand-name "orphan" drug products was established by the Orphan Drug Act of 1983. Moreover, exclusivity extensions are available for certain pediatric-related uses of drug products, and for qualifying antibiotic drug products. The FDA administers all of these exclusivities, which include:

- **Five-Year New Chemical Entity.** This exclusivity applies to a brand-name drug that contains a new chemical entity (NCE), which is a drug substance that contains an active ingredient or moiety(ies) never previously approved by the FDA. This exclusivity generally blocks the submission of any ANDA that contains the same active moiety for five years.

- **Three-Year New Clinical Studies**. This exclusivity attaches to a brand-name drug approved for a new use for a previously approved drug product. Applications for such new uses must be supported by information from new clinical investigations essential to approval of the new use and conducted or sponsored by the applicant. Such new uses could include changes in strength, dosage form, route of administration, or indication.

- **Orphan Drug**. Certain drugs designated for the treatment of a rare disease or condition (e.g., one affecting fewer than 200,000 people in the United States each year) are eligible for orphan-drug exclusivity upon approval. This exclusivity prevents approval of any other application (brand-name or generic) for the same drug for the same orphan-protected use during a seven-year period.

- **Pediatric**. This type of exclusivity is granted to a brand-name drug for which pediatric clinical studies have been conducted in response to a written request for such studies from the agency. Generally, pediatric exclusivity attaches to existing patents or exclusivities associated with the product line for the brand-name drug for six months.

- **GAIN**. The "Generating Antibiotic Incentives Now" (GAIN) exclusivity generally provides for an additional five years of exclusivity added to certain other exclusivity periods for a drug product that has been granted a "Qualified Infectious Disease Product" designation by the FDA.

- **180-Day**. This type of exclusivity may be granted to the first generic applicant(s) to submit a substantially complete ANDA that contains a challenge to a patent listed in the Orange Book. The generic drug applicant found to be eligible for this exclusivity has an exclusive right to market the generic drug for 180 days. Only ANDAs are eligible for this exclusivity.

New Chemical Entity Exclusivity

A new chemical entity means "a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the Act." The FDA's regulations define active moiety as the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

For five years after an NDA covering an NCE is approved, the FDA will not consider a request by another party for approval of that NCE either alone or in combination with other active molecules. Thus, more than five years of exclusivity is effectively possible. However, if made with a certification of patent invalidity or non-infringement, an application for approval of that NCE by another party may be submitted after four years.

As such, an ANDA filed with a Paragraph IV certification can be filed at the end of year four following approval of the drug. The first company or companies to submit an application that (1) is determined by the agency to be "substantially complete" upon submission and (2) contains a Paragraph IV certification to at least one of the patents listed in the Orange Book is generally eligible for the exclusive right to market the generic drug for 180 days. Over the years, many generic drug manufacturers have been actively filing ANDAs at the end of four years following approval of the drug with an intention to gain such "first filer" status. This report provides a summary of select new chemical entities that were approved in the year 2014 for which a generic drug manufacturer might plan to submit an ANDA with a Paragraph IV certification during the year 2018 to gain the first filer status.

2014 Novel New Drugs

In calendar year 2014, the FDA's Center for Drug Evaluation and Research (CDER) approved 41 novel new drugs as new molecular entities (NMEs) under New Drug Applications (NDAs) or as new therapeutic biologics under Biologics License Applications (BLAs). More than one-third of the novel new drugs approved in 2014 (17 of 41 or about 41%) were identified as First-in-Class and about 41% of the novel new drugs approved in 2014 (17 of 41) were approved to treat rare or "orphan" diseases.

CDER utilized the following four expedited development and review pathways:

> Fast Track, meaning drugs with the potential to address unmet medical needs. Fast Track speeds new drug development and review, for instance, by increasing the level of communication FDA allocates to drug developers and by enabling CDER to review portions of a drug application ahead of the submission of the complete application.

Breakthrough therapies, meaning drugs with preliminary clinical evidence demonstrating that the drug may result in substantial improvement on at least one clinically significant endpoint (i.e., study result) over other available therapies. A breakthrough therapy designation includes all of the Fast Track program features, as well as more intensive FDA guidance on an efficient drug development program. Breakthrough status is designed to help shorten the development time of a promising new therapy.

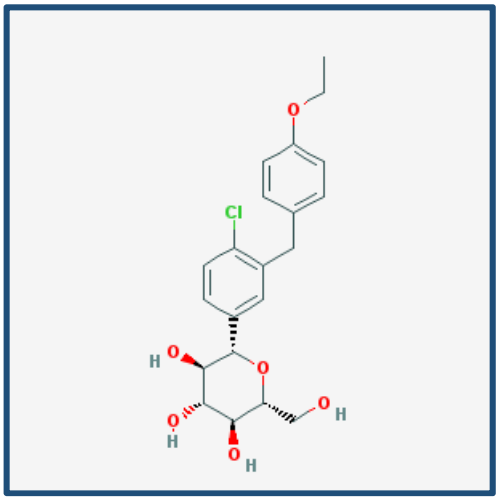
Priority Review, wherein the drug is determined to potentially provide a significant advance in medical care and set a target to review the drug within six months instead of the standard ten months.

Accelerated Approval program, which allows early approval of a drug for a serious or life-threatening illness that offers a benefit over current treatments. This approval is based on a "surrogate endpoint" (e.g., a laboratory measure) or other clinical measure that we consider reasonably likely to predict a clinical benefit of the drug. Once Accelerated Approval is granted, the drug must undergo additional testing to confirm that benefit; this speeds the availability of the drug to patients who need it.

Based on the above, CDER designated 41% as fast track, 22% as breakthrough therapies, 61% as priority review and 20% under FDA's Accelerated Approval program. Further, a majority of the novel new drugs of 2014 (32 of 41, 78%) were approved on the "first cycle" of review, meaning without requests for additional information that would delay approval and lead to another cycle of review.

Highlighted on the next page is a list of all of CDER's novel new drugs of 2014.

Proprietary Name	Established Name	Approval Date	Applicant Holder
Farxiga	dapaglifozin	08-Jan-14	Astrazeneca AB
Hetlioz	tasimelteon	31-Jan-14	Vanda Pharmaceuticals Inc.
Northera	droxidopa	18-Feb-14	Chelsea Therapeutics Inc.
Myalept	metreleptin for injection	24-Feb-14	Bristol-Myers Squibb Company
Impavido	miltefosine	19-Mar-14	Profounda Inc.
Neuraceq	florbetaben F 18 injection	19-Mar-14	Piramal Imaging SA
Otezla	apremilast	21-Mar-14	Celgene Corp
Zykadia	ceritinib	29-Apr-14	Novartis Pharmaceuticals Corp
Zontivity	vorapaxar	08-May-14	Merck Sharp and Dohme Corp
Dalvance	dalbavancin	23-May-14	Durata Therapeutics International BV
Jublia	efinaconazole	06-Jun-14	Dow Pharmaceutical Sciences
Sivextro (tablet) Sivextro (injection)	tedizolid phosphate	20-Jun-14	Cubist Pharmaceuticals Inc
Beleodaq	belinostat	03-Jul-14	Spectrum Pharmaceuticals Inc
Kerydin	tavaborole	07-Jul-14	Anacor Pharmaceuticals Inc
Zydelig	idelalisib	23-Jul-14	Gilead Sciences Inc
Striverdi Respimat	olodaterol	31-Jul-14	Boehringer Ingelheim Pharmaceuticals Inc
Jardiance	empagliflozin	01-Aug-14	Boehringer Ingelheim Pharmaceuticals Inc
Orbactiv	oritavancin	06-Aug-14	The Medicines Co.
Belsomra	suvorexant	13-Aug-14	Merck Sharp and Dohme Corp
Cerdelga	eliglustat	19-Aug-14	Genzyme Corp
Movantik	naloxegol	16-Sep-14	Astrazeneca Pharmaceuticals LP
Akynzeo	netupitant and palonosetron	10-Oct-14	Helsinn Helathcare SA
Harvoni	ledipasvir/sofosbuvir	10-Oct-14	Gilead Sciences Inc
Lumason	sulfur hexafluoride lipid microsphere	10-Oct-14	Bracco DIagnostics Inc.
Esbriet	pirfenidone	15-Oct-14	Intermune Inc
Ofev	nintedanib	15-Oct-14	Boehringer Ingelheim Pharmaceuticals Inc
Xtoro	finafloxacin otic suspension	17-Dec-14	Alcon Research Ltd
Lynparza	olaparib	19-Dec-14	Astrazeneca Pharmaceuticals LP
Rapivab	peramivir	19-Dec-14	Biocryst Pharmaceuticals Inc
Viekira Pak	(ombitasvir, paritaprevir and ritonavir tablets co-packaged with dasabuvir tablets)	19-Dec-14	Abbvie Inc
Zerbaxa	ceftolozane/tazobactam	19-Dec-14	Cubist Pharmaceuticals Inc



1. FARXIGA

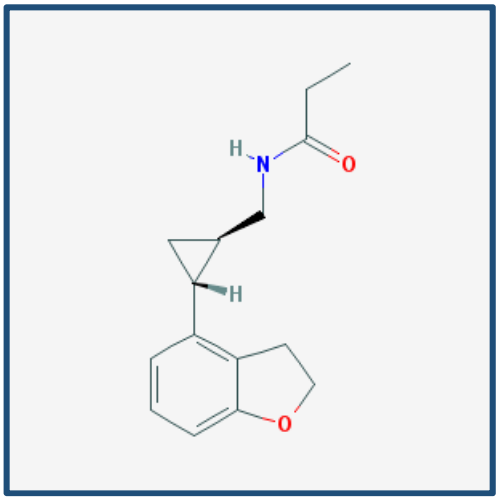
Active Ingredient: **DAPAGLIFLOZIN PROPANEDIOL**
Application Number: **N202293**
Approval Date: **Jan 8, 2014**
Applicant Holder: **ASTRAZENECA AB**

FARXIGA is a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated to improve glycemic control in adults with type 2 diabetes mellitus

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
20-25	M-157, NCE; M-212	18

OB Patents	Exp. Date	Claims are directed to
6,414,126	04-Oct-20	Compound; Pharmaceutical Composition; Method for treatment
6,515,117	04-Oct-20	Compound; Pharmaceutical Composition; Method for treatment
6,936,590	04-Oct-20	Method for treatment
7,456,254	30-Jun-25	Pharmaceutical Composition; Method for treatment
7,851,502	19-Aug-28	Pharmaceutical Composition
7,919,598	16-Dec-29	Crystalline compound; Process for preparing the same
8,221,786	21-Mar-28	Immediate release pharmaceutical formulation
8,329,648	18-Aug-26	Method for treatment
8,361,972	21-Mar-28	Method for treatment
8,431,685	13-Apr-25	Injectable composition; Method for treatment
8,461,105	13-Apr-25	Injectable composition; Method for treatment
8,501,698	20-Jun-27	Pharmaceutical Composition; Method for treatment
8,685,934	26-May-30	Method for treatment
8,716,251	21-Mar-28	Immediate release pharmaceutical formulation
8,721,615	18-Jan-30	An ampoule and an ampoule holder
8,906,851	18-Aug-26	Method for treatment comprising exendin-4
9,198,925	04-Oct-20	Method for treatment
9,238,076	15-Apr-24	Pharmaceutical Composition; Method for treatment

Critical patents expire in October 2020, including compound patents relating to dapagliflozin. Many more patents remain, however, directed to both immediate and sustained release formulations, crystal forms, methods of treatment, etc. With this many patents in play (and many potential co-defendants if the number of DMFs filed are an indication), litigation could be protracted.



2. HETLIOZ

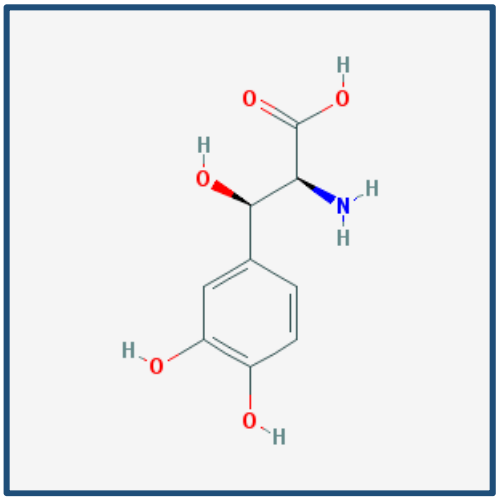
Active Ingredient: **TASIMELTEON**
Application Number: **N205677**
Approval Date: **Jan 31, 2014**
Applicant Holder: **VANDA PHARMACEUTICALS INC**

HETLIOZ is a melatonin receptor agonist indicated for the treatment of Non 24-Hour Sleep-Wake Disorder

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; ODE-59	7

OB Patents	Exp. Date	Claims are directed to
5,856,529	09-Dec-18	Compounds, Compositions, Methods of Treatment
9,060,995	25-Jan-33	Method of entraining a light perception impaired patient
9,539,234	25-Jan-33	Method of treating a patient for a circadian rhythm disorder
9,549,913	25-Jan-33	Method of entraining a patient's cortisol circadian rhythm
9,730,910	17-May-34	Method of treating a patient for a circadian rhythm disorder
9,855,241	25-Jan-33	Method of synchronizing a patient's abnormal cortisol circadian rhythm
RE46604	25-Jan-33	Method of entraining a patient suffering from Non-24

In only a few short months, the only patents that will remain on tasimelteon will be method patents. “Skinny” labeling may help, and pursuing anticipation and obviousness arguments for the various methods could be an option.



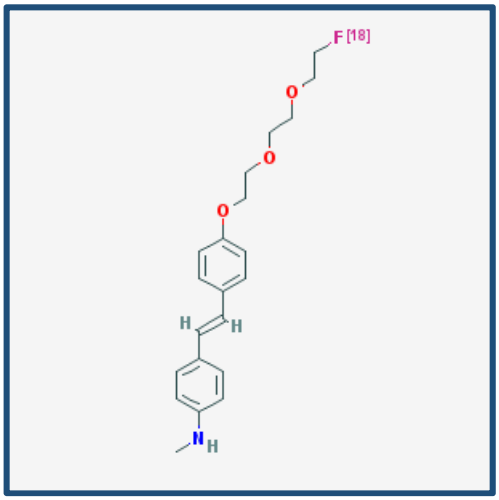
3. NORTHERA

Active Ingredient: **DROXIDOPA**
Application Number: **N203202**
Approval Date: **Feb 18, 2014**
Applicant Holder: **LUNDBECK NA LTD**

NORTHERA is indicated for the treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic neurogenic orthostatic hypotension (nOH) caused by primary autonomic failure (Parkinson's disease [PD], multiple system atrophy, and pure autonomic failure, dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
5-10	NCE; ODE-61	0

OB Patents	Exp. Date	Claims are directed to
There are no unexpired patents for this product in the Orange Book database.		



4. NEURACEQ

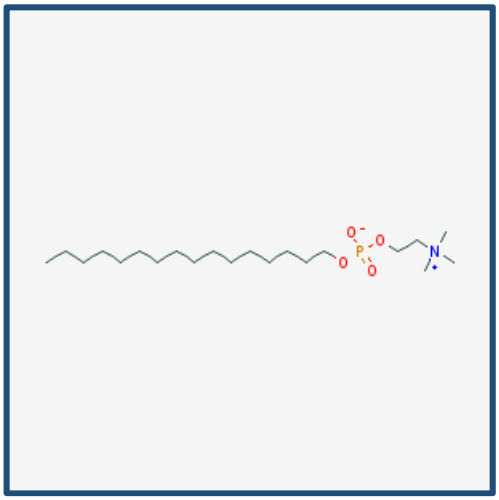
Active Ingredient: **FLORBETABEN F-18**
Application Number: **N204677**
Approval Date: **Mar 19, 2014**
Applicant Holder: **PIRAMAL IMAGING SA**

NEURACEQ is a radioactive diagnostic agent indicated for Positron Emission Tomography (PET) imaging of the brain to estimate β-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE	1

OB Patents	Exp. Date	Claims are directed to
7,807,135	18-Mar-29	Compound, Composition, Method of imaging amyloid deposits

Compound claims may deter generics, particularly when coupled with the need to comply with radioactivity regulations for florbetaben F-18.



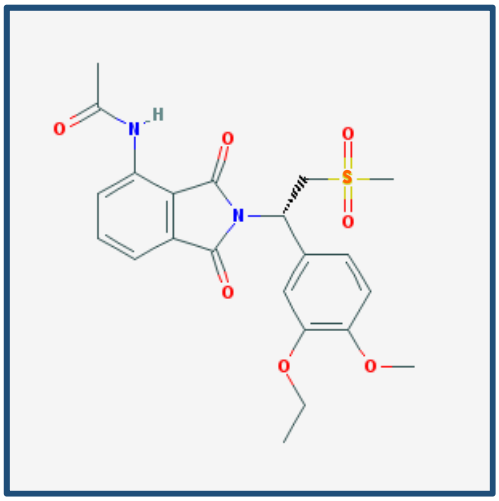
5. IMPAVIDO

Active Ingredient: **MILTEFOSINE**
Application Number: **N204684**
Approval Date: **Mar 19, 2014**
Applicant Holder: **KNIGHT THERAPEUTICS USA INC**

IMPAVIDO is an antileishmanial drug indicated in adults and adolescents ≥12 years of age weighing ≥30 kg (66 lbs) for treatment of: Visceral leishmaniasis due to Leishmania donovani; Cutaneous leishmaniasis due to Leishmania braziliensis, Leishmania guyanensis, and Leishmania panamensis; Mucosal leishmaniasis due to Leishmania braziliensis.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; ODE-63	0

OB Patents	Exp. Date	Claims are directed to
There are no unexpired patents for this product in the Orange Book database.		



6. OTEZLA

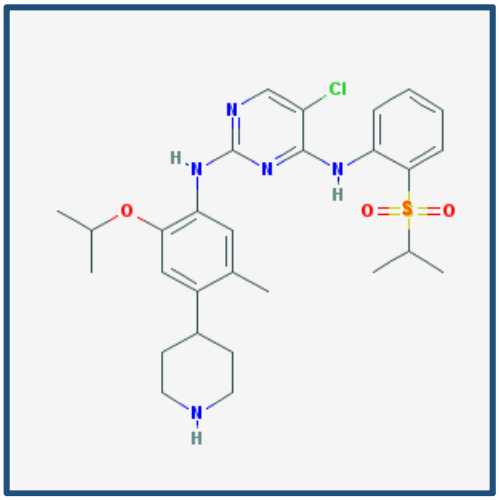
Active Ingredient: **APREMILAST**
Application Number: **N205437**
Approval Date: **Mar 21, 2014**
Applicant Holder: **CELGENE CORP**

OTEZLA is indicated for the treatment of certain types of psoriasis and psoriatic arthritis.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
20-25	NCE	10

OB Patents	Exp. Date	Claims are directed to
6,020,358	30-Oct-18	Compound, Method of inhibiting PDE IV, composition
6,962,940	19-Mar-23	Method of treating diseases or disorders ameliorated by the inhibition of PDE4
7,208,516	19-Mar-23	Method of treating psoriatic arthritis
7,427,638	17-Nov-24	Composition, Dosage form, Stereoisomer
7,659,302	19-Mar-23	Method of treating depression
7,893,101	09-Dec-23	Crystal Forms, composition
8,455,536	19-Mar-23	Method of treating psoriasis; rheumatoid arthritis; Behcet's Disease
8,802,717	19-Mar-23	Method of treating an arthritic condition
9,018,243	19-Mar-23	Method of treating a disease or disorder
9,872,854	29-May-34	Method of treating psoriatic arthritis

A critical compound patent expires in October 2018 to the apremilast family of compounds. Many patents remain, however, including those directed to stereoisomers, pharmaceutical compositions, crystal forms, methods of treatment, etc. Quick settlements still might occur given the relatively early expiration of most of the remaining patents. A lot of DMF filers may indicate that any ANDA litigation will involve multiple co-defendants who can share the burdens of litigation.



7. ZYKADIA

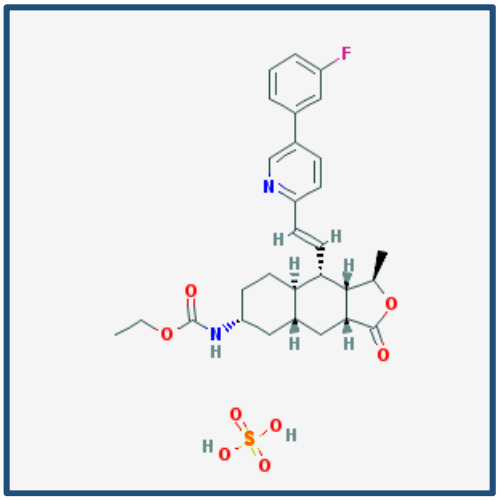
Active Ingredient: **CERITINIB**
Application Number: **N205755**
Approval Date: **Apr 29, 2014**
Applicant Holder: **NOVARTIS PHARMACEUTICALS CORP**

ZYKADIA is a kinase inhibitor indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; M-199; ODE-66; ODE-145	12

OB Patents	Exp. Date	Claims are directed to
7,153,964	26-Feb-21	Pyrimidine Compound; process for making; composition
7,893,074	25-Apr-26	Compound, Composition, Combo, Method of treating breast cancer
7,964,592	13-Jan-27	Compound, Composition, Combo, Method of treating breast cancer
8,039,479	29-Jun-30	Compound, Composition, Combo,
8,188,276	31-Jan-23	Compound; Method of treatment
8,377,921	20-Nov-27	Method of treatment
8,399,450	20-Nov-27	Compound; Composition
8,703,787	02-Feb-32	Method of treatment
8,835,430	31-Jan-23	Compound; Composition
9,018,204	31-Jan-23	Compound; Composition
9,309,229	18-Jan-32	Crystal Forms; Method of prep; composition
9,416,112	31-Jan-23	Compound

Multiple layers of compound patents cover ceritinib, as well as patents for methods of treatments, compositions, crystal forms, etc. Prolonged litigation, or litigation focusing on the later-expiring patents, would be expected.



8. ZONTIVITY

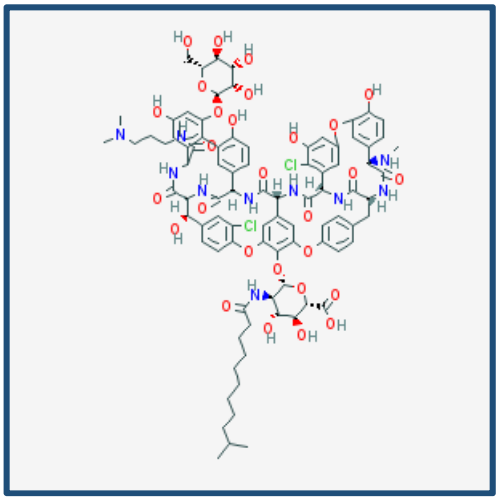
Active Ingredient: **VORAPAXAR SULFATE**
Application Number: **N204886**
Approval Date: **May 8, 2014**
Applicant Holder: **ARALEZ PHARMACEUTICALS TRADING DAC**

ZONTIVITY is a protease-activated receptor-1 (PAR-1) antagonist indicated for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease (PAD). ZONTIVITY has been shown to reduce the rate of a combined endpoint of cardiovascular death, MI, stroke, and urgent coronary revascularization.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE	2

OB Patents	Exp. Date	Claims are directed to
7,235,567	13-Jun-21	Polymorph; Composition
7,304,078	06-Apr-24	Compound; Composition; Method of Treatment

While only two patents are listed in the Orange Book, vorapaxar sulfate is protected by compound claims even if the polymorph claims can be designed around. .



9. DALVANCE

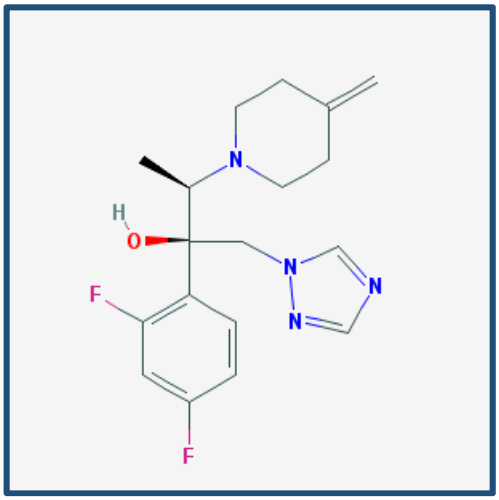
Active Ingredient: **DALBAVANCIN HYDROCHLORIDE**
Application Number: **N021883**
Approval Date: **May 23, 2014**
Applicant Holder: **ALLERGAN SALES LLC**

DALVANCE is indicated for acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible strains of Gram-positive microorganisms.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	D-154; NCE; NCE* GAIN	4

OB Patents	Exp. Date	Claims are directed to
6,900,175	25-Dec-23	Method for treating a bacterial infection
7,115,564	14-Nov-23	Dosage Form
7,119,061	14-Nov-23	Formulation
8,143,212	14-Nov-23	Method for treating a bacterial infection

"GAIN" exclusivity adds five additional years of market exclusivity, consuming the remainder of the term for the Orange Book patents covering dalbavancin.



10. JUBLIA

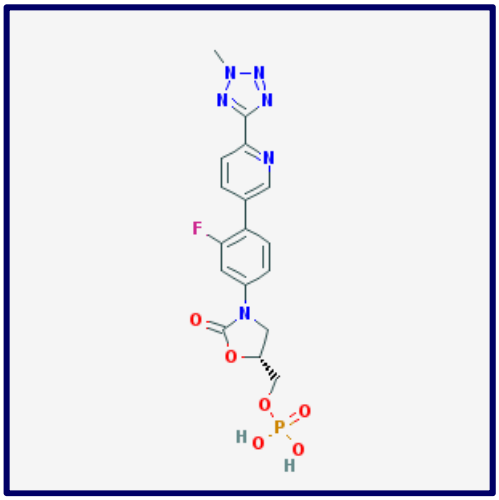
Active Ingredient: **EFINACONAZOLE**
Application Number: **N203567**
Approval Date: **Jun 6, 2014**
Applicant Holder: **DOW PHARMACEUTICAL SCIENCES**

JUBLIA is an azole antifungal indicated for the topical treatment of onychomycosis of the toenails due to Trichophyton rubrum and Trichophyton mentagrophytes.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
10-15	NCE	8

OB Patents	Exp. Date	Claims are directed to
7,214,506	05-Oct-21	Method for treating a subject having onychomycosis
8,039,494	08-Jul-30	Method for the treatment of a disorder of the nail or nail bed
8,486,978	24-Oct-30	Composition
9,302,009	24-Oct-30	Composition
9,566,272	03-Jan-28	Method for the treatment of onychomycosis
9,662,394	02-Oct-34	Composition
9,861,698	08-Jul-30	Method of treating a fungal infection
9,877,955	03-Jan-28	Method for the treatment of onychomycosis

Formulation patents and method of treatment patents, rather than compound patents, cover Jublia, making this drug a target for design-around strategies, carve-outs, and invalidity challenges. The number of DMFs filed suggests that multi-defendant NCE-1 litigation is likely to occur.



11. SIVEXTRO

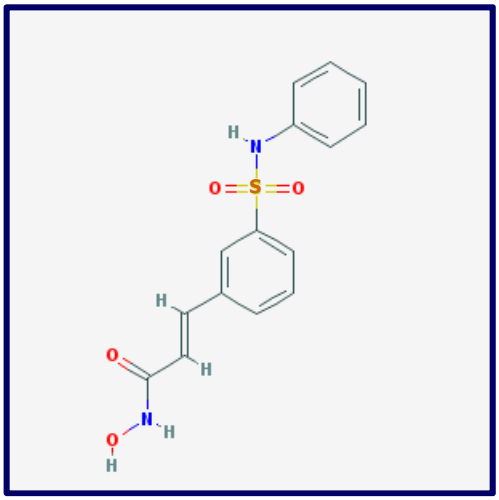
Active Ingredient: **TEDIZOLID PHOSPHATE**
Application Number: **N205436**
Approval Date: **Jun 20, 2014**
Applicant Holder: **CUBIST PHARMACEUTICALS LLC**

SIVEXTRO is an oxazolidinone-class antibacterial drug indicated in adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; NCE *GAIN	3

OB Patents	Exp. Date	Claims are directed to
7,816,379	23-Feb-28	Compound; Methods of preparation
8,420,676	23-Feb-28	Compound; Method of treating a bacterial infection
8,426,389	31-Dec-30	Crystalline particles, Compositions; Method of treating bacterial infection

While its “GAIN” exclusivity adds five additional years of market exclusivity, the patents covering Sivextro will still be at play after market exclusivity expires.



12. BELEODAQ

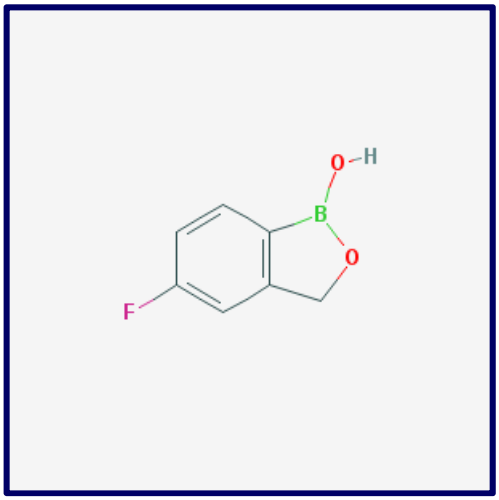
Active Ingredient: **BELINOSTAT**
Application Number: **N206256**
Approval Date: **Jul 3, 2014**
Applicant Holder: **SPECTRUM PHARMACEUTICALS INC**

BELEODAQ is a histone deacetylase inhibitor indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; ODE-68	2

OB Patents	Exp. Date	Claims are directed to
6,888,027	27-Sep-21	Compound; Composition; Method of inhibiting cell proliferation
8,835,501	27-Oct-27	Composition; Kit

Once the '027 patent expires, there will be only one patent standing in the way of generic belinostat. The broad composition claims of that patent may still be an obstacle, however.



13. KERYDIN

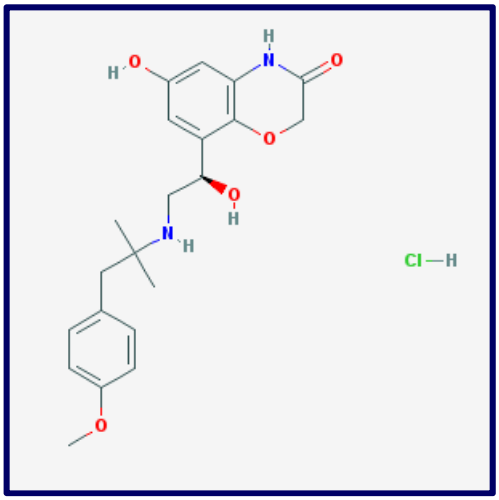
Active Ingredient: **TAVABOROLE**
Application Number: **N204427**
Approval Date: **Jul 7, 2014**
Applicant Holder: **ANACOR PHARMACEUTICALS INC**

KERYDIN is an oxaborole antifungal indicated for the topical treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE	5

OB Patents	Exp. Date	Claims are directed to
7,582,621	26-May-27	Method of treating an infection
9,549,938	16-Feb-26	Method of treating a Tinea unguium infection
9,566,289	16-Feb-26	Formulation
9,566,290	16-Feb-26	Method of treating a human having onychomycosis of a toenail
9,572,823	16-Feb-26	Method of delivering a compound

The '621 patent was invalidated by the U.S. Patent Trial and Appeal Board in an *inter partes* review proceeding initiated by the Coalition for Affordable Drugs. Federal Circuit review is pending -- the outcome may impact litigation strategy on the remaining patents.



14. STRIVERDI RESPIMAT

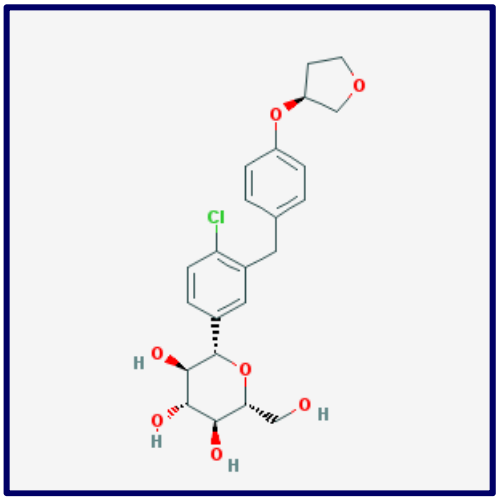
Active Ingredient: **OLODATEROL HYDROCHLORIDE**
Application Number: **N203108**
Approval Date: **Jul 31, 2014**
Applicant Holder: **BOEHRINGER INGELHEIM PHARMACEUTICALS INC**

STRIVERDI RESPIMAT is a long-acting beta$_2$-adrenergic agonist indicated for the long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE	18

OB Patents	Exp. Date	Claims are directed to
6,846,413	28-Aug-18	Filter, Nebulizer
6,977,042	28-Aug-18	Filter, Nebulizer
6,988,496	23-Feb-20	Cartridge for a liquid
7,056,916	07-Dec-23	Compound; Composition
7,220,742	12-May-25	Compound; Method for the treatment of respiratory complaints
7,284,474	26-Aug-24	Piston pumping system
7,396,341	10-Oct-26	Blocking Device
7,491,719	10-Nov-23	Compounds
7,727,984	10-Nov-23	Compounds
7,786,111	10-Nov-23	Compositions
7,802,568	26-Feb-19	Releasable Connection
7,837,235	13-Mar-28	Apparatus
7,896,264	26-May-25	Microstructured nozzle
7,988,001	04-Aug-21	Container
8,034,809	12-May-25	Method for the treatment of respiratory complaints
8,044,046	10-Nov-23	Method for the treatment of COPD
8,733,341	16-Oct-30	Atomizer; Method for delivering and atomizing fluid
9,027,967	31-Mar-27	Apparatus

Multiple patents covering the inhalation device and delivery method itself may create an extra hurdle for some generics wanting to market olodaterol hydrochloride.



15. JARDIANCE

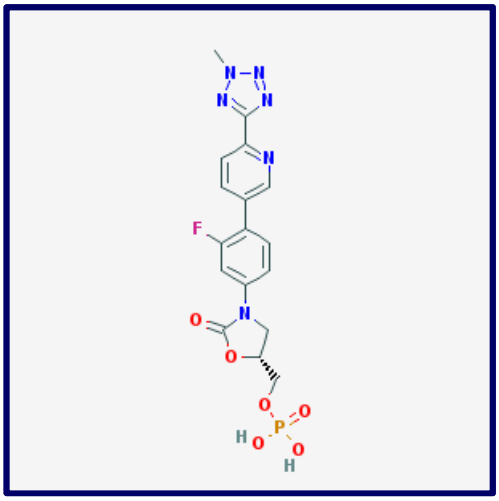
Active Ingredient: **EMPAGLIFLOZIN**
Application Number: **N204629**
Approval Date: **Aug 1, 2014**
Applicant Holder: **BOEHRINGER INGELHEIM PHARMACEUTICALS INC**

JARDIANCE is a sodium-glucose co-transporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
5-10	M-160; M-161; M-174; NCE; I-739	3

OB Patents	Exp. Date	Claims are directed to
7,579,449	05-Nov-25	Compounds
7,713,938	15-Apr-27	Crystal Forms
8,551,957	14-Oct-29	Compositions; Method for improving glycemic control

Multiple co-defendants in an ANDA litigation would be predicted for empagliflozin given the number of DMF filers. The group faces a traditional trio of patents with compound claims relating to empagliflozin as well as claims to crystal forms, compositions, and methods of treatment.



16. ORBACTIV

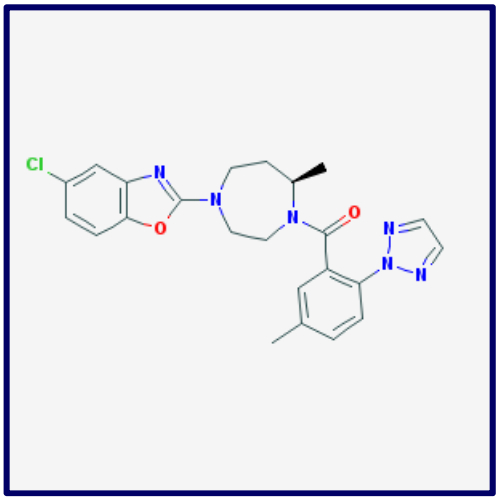
Active Ingredient: **ORITAVANCIN DIPHOSPHATE**
Application Number: **N206334**
Approval Date: **Aug 6, 2014**
Applicant Holder: **MELINTA SUBSIDIARY CORP**

ORBACTIV is a lipoglycopeptide antibacterial drug indicated for the treatment of adult patients with acute bacterial skin and skin structure infections caused or suspected to be caused by susceptible isolates of designated Gram-positive microorganisms.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; NCE *GAIN	3

OB Patents	Exp. Date	Claims are directed to
8,420,592	29-Aug-29	Method of treating a complicated skin and skin structure infection
9,649,352	16-Jul-35	Compositions
9,682,061	26-Apr-30	Method of treating a bacterial infection

"GAIN" exclusivity adds five additional years of market exclusivity, but the patents covering Orbactiv will still have many years left after that exclusivity expires.



17. BELSOMRA

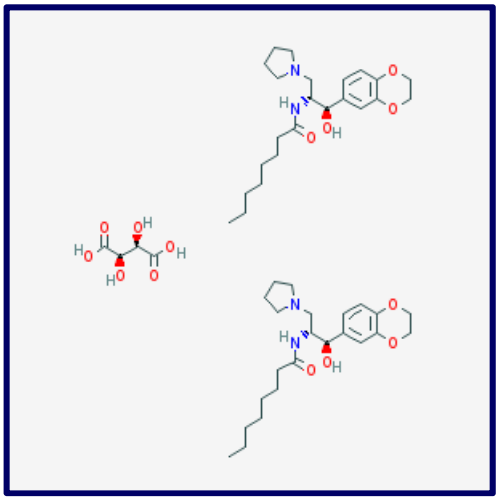
Active Ingredient: **SUVOREXANT**
Application Number: **N204569**
Approval Date: **Aug 13, 2014**
Applicant Holder: **MERCK SHARP AND DOHME CORP**

BELSOMRA is an orexin receptor antagonist indicated for the treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE	1

OB Patents	Exp. Date	Claims are directed to
7,951,797	20-Nov-29	Compound; Composition; Method for treating insomnia

The sole patent currently listed for suvorexan has not only compound claims, but has broad composition and method of treatment claims. An uphill battle may await.



18. CERDELGA

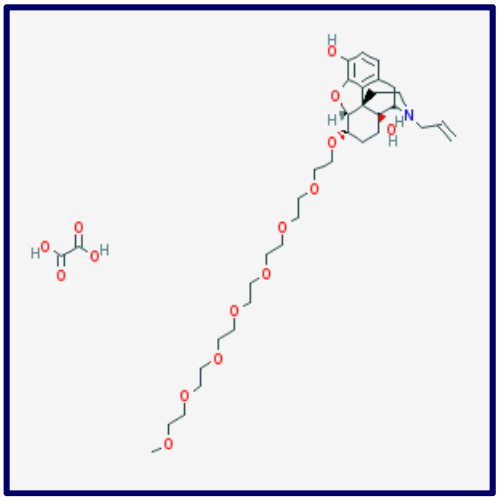
Active Ingredient: **ELIGLUSTAT TARTRATE**
Application Number: **N205494**
Approval Date: **Aug 19, 2014**
Applicant Holder: **GENZYME CORP**

CERDELGA is a glucosylceramide synthase inhibitor indicated for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; ODE-73	3

OB Patents	Exp. Date	Claims are directed to
6,916,802	29-Apr-22	Compound; Method for reducing tumor angiogenesis
7,196,205	29-Apr-22	Compounds
7,615,573	29-Apr-22	Method of inhibiting glucosylceramide synthase

The relatively early expiration date for the Orange Book patents likely will discourage ANDA litigation -- once time to trial and appeal is factored in, waiting for the patents to expire may be the more logical choice.



19. MOVANTIK

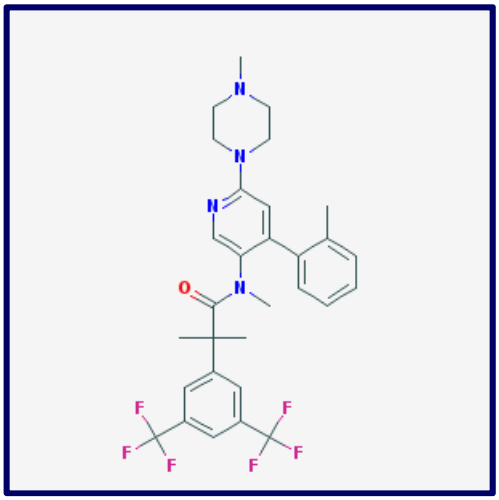
Active Ingredient: **NALOXEGOL OXALATE**
Application Number: **N204760**
Approval Date: **Sep 16, 2014**
Applicant Holder: **ASTRAZENECA PHARMACEUTICALS LP**

MOVANTIK is an opioid antagonist indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE	6

OB Patents	Exp. Date	Claims are directed to
7,056,500	29-Jun-24	Compositions: Method of treating a side effect of an opioid agonist
7,662,365	18-Oct-22	Polymer; Composition
7,786,133	19-Dec-27	Compounds; compositions
8,067,431	16-Dec-24	Method of treating a patient in need of an opioid antagonist
8,617,530	18-Oct-22	Method of treating constipation
9,012,469	02-Apr-32	Crystals; compositions

The polymeric aspect of naloxegol oxalate may help dissuade generic challenge along with the ’133 patent and ’469 patent covering the compound and crystalline forms, which have several years of patent term remaining.



20. AKYNZEO

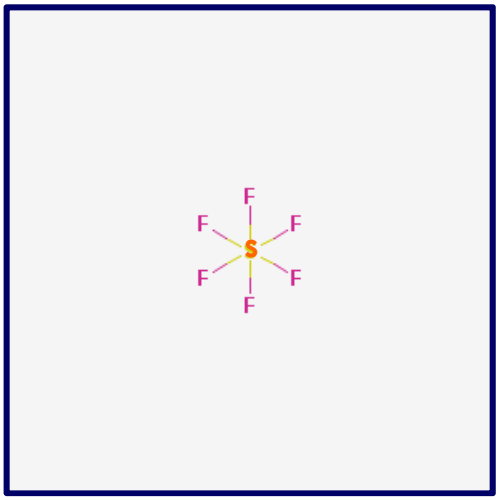
Active Ingredient: **NETUPITANT; PALONOSETRON HYDROCHLORIDE**
Application Number: **N205718**
Approval Date: **Oct 10, 2014**
Applicant Holder: **HELSINN HEALTHCARE SA**

AKYNZEO is a fixed combination of netupitant, a substance P/neurokinin 1 (NK1) receptor antagonist, and palonosetron, a serotonin-3 ($5\text{-}HT_3$) receptor antagonist indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Oral palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
20-25	NCE	5

OB Patents	Exp. Date	Claims are directed to
6,297,375	22-Feb-20	Compounds
8,623,826	18-Nov-30	Method of treating both nausea and vomiting
8,951,969	18-Nov-30	Oral dosage forms; compositions
9,186,357	18-Nov-30	Method of treating chemotherapy-induced nausea and vomiting
9,271,975	09-Sep-31	Method of achieving no emesis

The number of DMF filers indicates that Akynzeo will be a target for many generic drug companies. With compound claims expiring in February 2020, the focus of any ANDA litigation will be the combination of the active ingredients, dosage forms, and the many method claims.



21. LUMASON

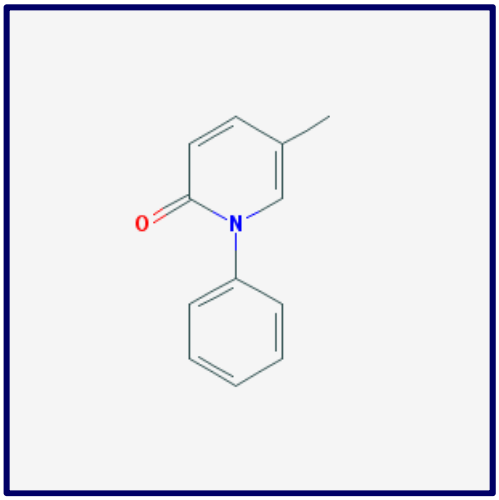
Active Ingredient: **SULFUR HEXAFLUORIDE LIPID-TYPE A MICROSPHERES**
Application Number: **N203684**
Approval Date: **Oct 15, 2014**
Applicant Holder: **BRACCO DIAGNOSTICS INC**

LUMASON is an ultrasound contrast agent indicated for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	I-728; NCE	1

OB Patents	Exp. Date	Claims are directed to
5,686,060	11-Nov-19	injectable suspension for ultrasonic echography

With expiration of the only Orange Book patent early next year**,** it is unlikely that ANDA litigation would proceed on Lumason.



22. ESBRIET

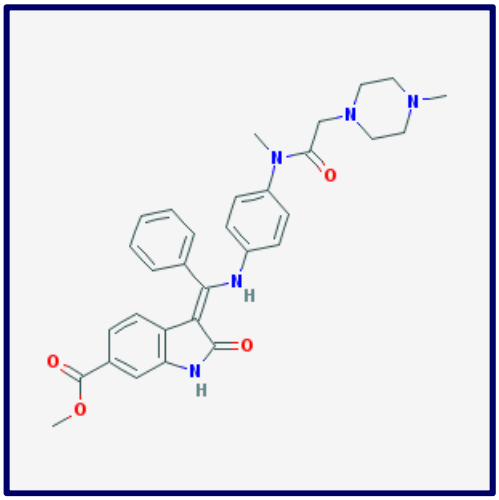
Active Ingredient: **PIRFENIDONE**
Application Number: **N022535**; N208780
Approval Date: **Oct 15, 2014**
Applicant Holder: **GENENTECH INC**

ESBRIET is a pyridone indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
10-15	NCE; ODE-77	19

OB Patents	Exp. Date	Claims are directed to
7,566,729	22-Apr-29	Method of treating a patient with idiopathic pulmonary fibrosis
7,635,707	22-Apr-29	Method of treating a patient with idiopathic pulmonary fibrosis
7,696,236	18-Dec-27	Method of treating a patient with idiopathic pulmonary fibrosis
7,767,225	22-Sep-26	Capsule formulation
7,767,700	18-Dec-27	Dose escalation regimen Method
7,816,383	08-Jan-30	Method of administering pirfenidone therapy
7,910,610	08-Jan-30	Method of administering pirfenidone therapy
7,988,994	22-Sep-26	Capsule formulation; Method for treating a fibrotic condition
8,013,002	08-Jan-30	Method of administering pirfenidone and fluvoxamine
8,084,475	08-Jan-30	Method of administering pirfenidone therapy
8,318,780	08-Jan-30	Method of administering pirfenidone therapy
8,383,150	22-Sep-26	Granulate formulation; Method for treating a fibrotic condition
8,420,674	18-Dec-27	Starter pack for use in an initial dose escalation regimen
8,592,462	22-Apr-29	Method of administering pirfenidone
8,609,701	22-Apr-29	Method of treating a patient in need of pirfenidone
8,648,098	08-Jan-30	Method of increasing the effectiveness of pirfenidone therapy
8,753,679	22-Sep-26	Capsule formulation
8,754,109	08-Jan-30	Method of increasing the effectiveness of pirfenidone therapy
8,778,947	30-Aug-33	Improved method of administering pirfenidone therapy

Multiple DMF filings indicate that pirfenidone will likely be a multi-defendant NCE-1 litigation. While many patents are listed in the Orange Book, none relate to the compound itself -- claims to formulation, administration, and dosing exist instead. Such claims can be susceptible to anticipation or obviousness challenges and may provide noninfringement opportunities as well.



23. OFEV

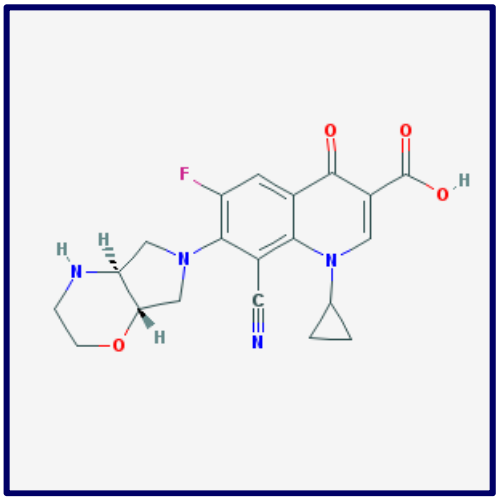
Active Ingredient: **NINTEDANIB ESYLATE**
Application Number: **N205832**
Approval Date: **Oct 15, 2014**
Applicant Holder: **BOEHRINGER INGELHEIM PHARMACEUTICALS INC**

OFEV is a kinase inhibitor indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; ODE-77	3

OB Patents	Exp. Date	Claims are directed to
6,762,180	10-Dec-20	Compounds, Salts & Compositions
7,119,093	21-Feb-24	Compounds; Crystals; Compositions
7,989,474	06-Apr-24	Method for treating lung fibrosis

Both the ’180 patent and the ’093 patent contain compound claims that appear to cover nintedanib, which may dissuade generic drug companies from pursuing ANDA litigation.



24. XTORO

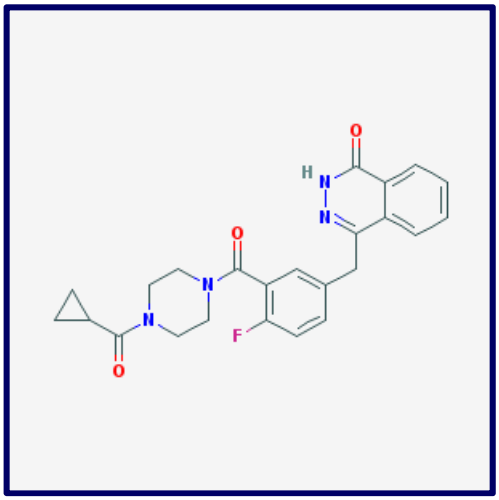
Active Ingredient: **FINAFLOXACIN**
Application Number: **N206307**
Approval Date: **Dec 17, 2014**
Applicant Holder: **NOVARTIS PHARMACEUTICALS CORP**

XTORO is a quinolone antimicrobial indicated for the treatment of acute otitis externa (AOE) caused by susceptible strains of Pseudomonas aeruginosa and Staphylococcus aureus.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; NCE *PED	3

OB Patents	Exp. Date	Claims are directed to
8,536,167	08-Aug-31	Method for treating an ophthalmic, otic, or nasal infection
9,119,859	02-Jul-30	Method for treating acute otitis externa or acute otitis media
9,504,691	21-Nov-33	Topical composition; Method for treating an ophthalmic, otic, or nasal infection

Focused on treatment methods and compositions, the patents covering finafloxacin have a significant amount of time remaining before they expire even after pediatric exclusivity is applied.



25. LYNPARZA

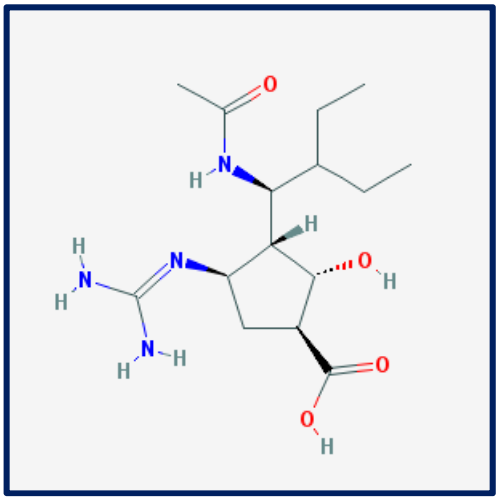
Active Ingredient: **OLAPARIB**
Application Number: **N206162; N208558**
Approval Date: **Dec 19, 2014**
Applicant Holder: **ASTRAZENECA PHARMACEUTICALS LP**

LYNPARZA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for: (1) the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy; (2) the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy; and (3) select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; ODE-83	7

OB Patents	Exp. Date	Claims are directed to
7,151,102	29-Apr-22	Compounds; Compositions
7,449,464	11-Oct-24	Compounds; Compositions
7,981,889	11-Oct-24	Compounds; Compositions
8,143,241	12-Aug-27	Method of treatment of cancer
8,247,416	24-Sep-28	Compounds
8,859,562	04-Aug-31	Method of treatment of cancer cells
8,912,187	12-Mar-24	Method of treatment for breast or ovarian cancer

Multiple layers of compound patents cover olaparib, as well as patents for methods of treatments and compositions. While some patent claims are vulnerable in their breadth, prolonged litigation, or litigation focusing on the later-expiring patents, would be expected.



26. RAPIVAB

Active Ingredient: **PERAMIVIR**
Application Number: **N206426**
Approval Date: **Dec 19, 2014**
Applicant Holder: **BIOCRYST PHARMACEUTICALS INC**

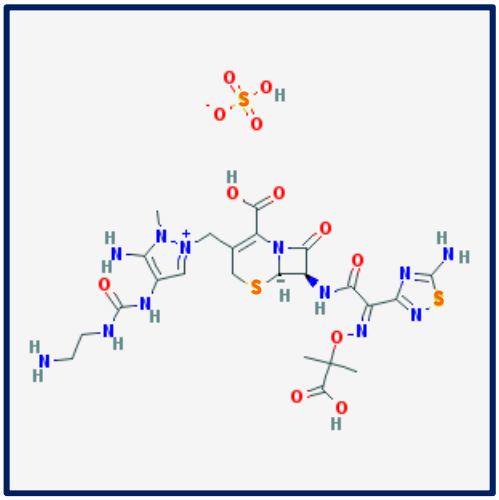
RAPIVAB is an influenza virus neuraminidase inhibitor indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than two days.

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
< 5	NCE; NPP	3

OB Patents	Exp. Date	Claims are directed to
6,503,745	05-Nov-19	Compound; Method of detecting influenza virus
6,562,861	17-Dec-18	Compound; Method of treating influenza virus
8,778,997	07-May-27	Method for treating a viral infection

Compound patents to peramivir expire by the end of 2019, leaving only one Orange Book patent with claims to a method of treating a viral infection to prevent generic entry.

27. ZERBAXA



Active Ingredient: **CEFTOLOZANE SULFATE; TAZOBACTAM SODIUM**
Application Number: **N206829**
Approval Date: **Dec 19, 2014**
Applicant Holder: **CUBIST PHARMACEUTICALS LLC**

ZERBAXA is a combination product consisting of a cephalosporin-class antibacterial drug and a beta-lactamase inhibitor indicated for the treatment of the following infections caused by designated susceptible microorganisms:

Complicated Intra-abdominal Infections, used in combination with metronidazole
Complicated Urinary Tract Infections, including Pyelonephritis

US DMFs Filed	USFDA Exclusivities	OB Listed Patents
10-15	NCE; NCE *GAIN	7

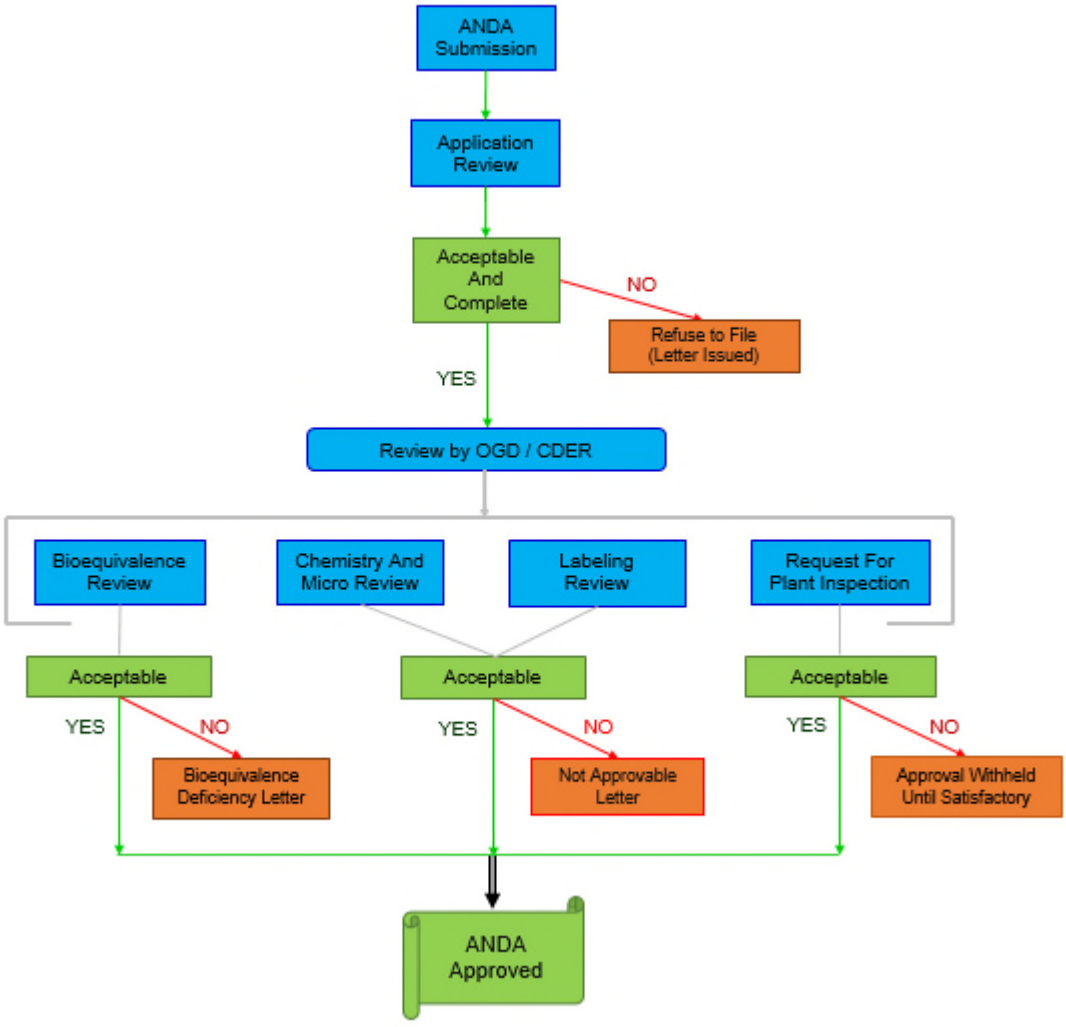
OB Patents	Exp. Date	Claims are directed to
7,129,232	21-Oct-24	Compounds
8,476,425	27-Sep-32	Composition
8,685,957	27-Sep-32	Method for the treatment of bacterial infections; Compositions
8,906,898	28-May-34	Solid Form 2 of ceftolozane sulfate; Compositions
8,968,753	14-Mar-34	Method of treating an infection
9,320,740	14-Mar-34	Pharmaceutical composition comprising tazobactam
9,872,906	14-Mar-34	Composition comprising ceftolozane sulfate and tazobactam sodium

The number of DMF filers indicates that Zerbaxa will be a target for many generic drug companies and produce a multi-defendant NCE-1 ANDA litigation. The Orange Book patents contain a wide variety of claims, relating not only to the compounds, but also compositions, solid forms, and methods of treatment. Sharing resources and information among co-defendants may prove helpful in getting a generic to market.

Good ANDA Submission Practices

As part of its Drug Competition Action Plan the FDA published a draft guidance on Jan. 3, 2018 detailing good practices for the submission of ANDAs. The guidance highlights common, recurring deficiencies that may lead to a delay in the approval of an ANDA and makes recommendations to applicants on how to avoid such deficiencies. A typical ANDA requires an average of four review cycles before approval. The delay happens when ANDAs are submitted without all the information that the FDA needs to determine whether the ANDA meets FDA standards for approval, which leads to additional review cycles.

- ANDA Approval Process



The draft guidance specifically addresses deficiencies commonly arising with respect to four components of ANDA submissions: (i) patents and exclusivities, (ii) labeling, (iii) product quality and (iv) bioequivalence. Highlighted below are some of the important takeaways from the draft guidance.

- **Patents and exclusivities:** the draft guidance highlighted that applicants often do not submit required information concerning the timely dispatch of a Paragraph IV notice letter, filing of a legal action by a patent owner, or failure by a patent owner to file any such legal action within the specified time frame. Also, when a new patent is listed for a Reference Listed Drug ("RLD"), applicants mistakenly file "serial submissions" of amendments to their Paragraph IV certifications before FDA regulations allow such amendment or, alternatively, fail to provide the requisite certification for a newly listed patent altogether. The draft guidance reiterated requirements regarding the following aspects related to their ANDA:

    A. Documentation and notification of a legal action filing
    B. Resolution or appeal of a legal action
    C. Notice of Paragraph IV certification
    D. New or revised information in the Orange book
    E. Amendments to an unapproved ANDA
    F. Notification of commercial marketing

- **Labeling:** the draft guidance highlighted that applicants have improperly submitted draft container labels that do not accurately portray the formatting factors used with the final printed labels. Also, that the applicants have submitted container labels with insufficient color differentiation for the different strengths of a drug product. For parenteral drug products, the guidance mentioned that the applicants have mistakenly proposed package types that differ from the type approved for the RLD. The draft guidance reiterated requirements regarding the following aspects related to their ANDA:

    A. Draft container labels and carton labeling
    B. Color differentiation for container labels and carton labeling
    C. Labeling format
    D. Parenteral drug products

- **Product quality deficiencies:** the draft guidance addressed common issues associated with in vitro dissolution (biopharmaceutics) and manufacturing facilities, among many other subtopics. For in vitro dissolution testing, applicants commonly omit solubility data for the full physiologic pH range, a detailed description of the proposed dissolution test for evaluation of the product (including developmental parameters used in selecting the proposed method), data demonstrating the dissolution method's discriminating ability, and complete dissolution data and information for all strengths of the test and reference products. For manufacturing facilities, the draft guidance mentioned that applicants have frequently neglected to provide complete information in their Form FDA 356h and in the correct modules within their applications.

    A. Drug substance, including API starting material, manufacturing process and impurities
    B. Drug product, including establishing critical quality attributes
    C. *In vitro* dissolution (biopharmaceutics)
    D. Facilities
    E. Commercial manufacturing process
    F. Microbiology considerations

- **Bioequivalence:** the draft guidance suggested that applicants include in their bioanalytical study reports complete dilution integrity data (as well as stock stability and recovery data), analytical raw data from all study runs, serially selected chromatograms (representing 20% of study subjects), and bioanalytical standard operating procedures. For differences in formulations and inactive ingredients, the draft guidance mentioned that applicants have sometimes failed to provide necessary justifications and documentation addressing these differences. If and when a different inactive ingredient or amount of an inactive ingredient was used in a placebo test formulation for bioequivalence testing, the applicant must explain why this change did not affect their showing of bioequivalence of the proposed drug product to the RLD. The draft guidance reiterated requirements regarding the following aspects related to their ANDA:

    A. Bioanalytical study data
    B. Clinical summary
    C. Deviations from product-specific guidances
    D. Information on bioequivalence and safety related to *in vivo* bioequivalence studies
    E. Differences in formulations and inactive ingredients
    F. Waiver requests under 12 CFR 314.99(b)

SEYFARTH SHAW

Atlanta	London	San Francisco
Boston	Los Angeles	Shanghai
Chicago	Melbourne	Sydney
Hong Kong	New York	Washington, D.C.
Houston	Sacramento	

www.seyfarth.com