IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

VALEANT PHARMACEUTICALS INTERNATIONAL, SALIX PHARMACEUTICALS LTD. and COSMO TECHNOLOGIES LIMITED,	)	
Plaintiffs,	)	
v.	)	C.A. No: 18-1288 (UNA)
ACTAVIS LABORATORIES FL., INC., ACTAVIS PHARMA, INC., TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICAL INDUSTRIES LTD.,	)	**JURY TRIAL DEMANDED**
Defendants.	)	REDACTED - PUBLIC VERSION

OPENING BRIEF IN SUPPORT OF PLAINTIFFS' MOTION FOR TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

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I. NATURE AND STAGE OF PROCEEDINGS

Pursuant to Fed. R. Civ. P. 65, Plaintiffs Valeant Pharmaceuticals International, Salix Pharmaceuticals Ltd., and Cosmo Technologies Limited, by and through their counsel, respectfully submit this brief in support of their motion for a temporary restraining order ("TRO") and preliminary injunction ("PI") to prevent Defendants Actavis Laboratories FL, Inc., Actavis Pharma Inc., Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Limited (collectively, "Actavis" or "Defendants") from manufacturing, offering to sell, or selling their generic version of budesonide extended-release tablets, for oral use, that is the subject of ANDA No. 205457 (the "Accused Product"), which infringes Cosmo's U.S. Patent No. 10,052,286 (the "'286 patent" or "Asserted Patent").[1]

II. SUMMARY OF ARGUMENT

Plaintiffs bring this motion to temporarily and preliminarily enjoin Actavis' recent at-risk launch of a generic version of Plaintiffs' Uceris® product, based on the '286 patent, which issued on August 21, 2018 and reads *verbatim* on Actavis' generic product as described in Actavis' package insert.

On February 17, 2015, Plaintiffs filed a patent infringement action under the Hatch-Waxman Act, 21 U.S.C. § 355(j), against Actavis, based on its submission of ANDA No. 205457 for its proposed generic version of Plaintiffs' Uceris® product.[2] Plaintiffs asserted a number of Orange Book-listed patents, but dropped their allegations of infringement for all but one of the

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[1] Valeant Pharmaceuticals International ("VPI") and Salix Pharmaceuticals Ltd. ("Salix") are subsidiaries of Bausch Health Companies Ltd. (formerly Valeant Pharmaceuticals International Inc.). For convenience, VPI and Salix will be collectively referred to herein as "Bausch," while Cosmo Technologies Limited will be referred to as "Cosmo," and all three collectively will be referred to as "Plaintiffs."

[2] *Cosmo Technologies Ltd. v. Actavis Laboratories FL, Inc.*, No. 15-164-LPS (D. Del.) (the "ANDA Litigation").

patents, U.S. Patent No. 8,784,888 (the "'888 patent"). After a bench trial, the Court ruled that Plaintiffs had failed to prove that Actavis' proposed generic product would infringe the asserted claims of the '888 patent. ANDA Litigation (Slip Op. at D.I. 272) (Oct. 2, 2017). Specifically, the Court found that Plaintiffs had failed to prove that Actavis' ANDA product has a "macroscopically homogenous composition," which was "the only claim limitation at issue." ANDA Litigation, D.I. 272 at 15. The Court entered final judgment in favor of Actavis; an appeal is pending before the Federal Circuit.

On July 6, 2018, Cosmo filed an additional suit against Actavis relating to infringement of U.S. Patent No. 9,737,489 ("the '489 patent"), and U.S. Patent No. 9,592,203 ("the '203 patent") by Actavis' generic product.[3] Because of the similarity of the asserted claims in that action to the claims of the '888 patent, the parties are discussing staying that case pending the results of the appeal of the first action.

On July 9, 2018, Defendants announced the at-risk launch of their generic version of Uceris®. Complaint, Ex. 4 (Teva's Press Release). The '286 patent is directed to a 9 mg budesonide extended release formulation consisting essentially of a tableted core matrix and a composition of certain excipients covered by a gastro-resistant film coating. Plaintiffs bring this action to assert the '286 patent, a new patent which issued on August 21, 2018, and seek preliminary injunctive relief to enjoin Defendants' marketing and sale of their Accused Product.

The asserted claims of the '286 patent do not contain the "macroscopically homogeneous composition" limitation which formed the basis for the Court's finding of non-infringement in the first case. To the contrary, the '286 patent is from a different patent family than the '888 patent, and each and every limitation of the asserted claims reads *verbatim* on

[3] *Cosmo Technologies Ltd. v. Actavis Laboratories FL, Inc.*, No. 18-1006-LPS (D. Del.).

Actavis' generic Uceris product as described in Actavis' publicly-available product label. Thus, for example, the '286 patent claims a tableted core "matrix," which Actavis' product label explicitly states it has. *See* Complaint, Ex. 5 ("Actavis Label") at 8 ("Upon disintegration of the coating, the ***core matrix*** provides extended-release of budesonide in a time dependent manner.") (emphasis added). Similarly, the '286 patent claims recite specific ingredients as well as certain pharmacokinetic values which are expressly set out in the product label.

In short, the new '286 patent does not suffer from any of the putative infirmities of the '888 patent and reads directly on the Accused Product. Plaintiffs thus will likely succeed on the merits of the infringement case. Moreover, because the '286 patent addresses the difficult problem of formulating an extended release budesonide tablet with optimal pharmacokinetic (PK) parameters for the treatment of ulcerative colitis, Plaintiffs are likely to succeed against any validity challenge brought by Actavis.

Plaintiffs will also suffer irreparable harm if Actavis' at-risk launch of its generic Uceris® product is not enjoined. Actavis' six weeks of sales of the Accused Product has already caused real and severe harm to Plaintiffs, which, if not enjoined promptly, will become irreparable. For example, Defendants' continued sales of its Accused Product will: (1) destroy one of Plaintiffs' most important brands and primary revenue sources; (2) permanently decrease the market price of Uceris® and drastically erode Plaintiffs' market share; (3) weaken Plaintiffs' ability to fund, develop and bring to market new drugs in its pipeline; (4) [redacted]; and (5) irrevocably damage the goodwill Plaintiffs have built.

In contrast to the irreparable damage to Plaintiffs, the potential harm to Defendants resulting from a TRO or PI is far less. Given the fact that Defendants have only recently

launched their product, a TRO and PI will only return the parties to the *status quo ante* pending the resolution of the infringement claims. The balance of the harms, therefore, weighs in favor of returning the parties to the status quo until this lawsuit is concluded. And the public interest weighs in favor of enjoining an at-risk launch of generic products until the generic companies' right to sell the product has been fully adjudicated.

III. STATEMENT OF FACTS

A. TECHNOLOGY BACKGROUND

Ulcerative colitis ("UC") is a long-term condition that results in inflammation and ulcers of the colon and rectum. Byrn Decl. ¶17. The inflammation of the colon caused by ulcerative colitis can lead to bleeding, diarrhea, and abdominal or stomach pain, and in severe cases removal of the large intestine (which is another name for the colon). Byrn Decl. ¶ 17. Plaintiffs' invention, as claimed in the '286 patent, provides improved delivery methods for drugs that can alleviate ulcerative colitis and therefore improves quality-of-life for UC patients.

Treatment of UC using oral dosage forms presents challenges relating to preventing absorption of drugs in the upper GI tract,[4] and requires optimal PK parameters—achieving drug concentrations and oral bioavailability at the right level and at the right time—associated with colonic release. Byrn Decl. ¶¶ 18-19. PK depends in part on the tablet coating and the excipients used in the formulation. Optimal PK for treatment of UC with budesonide requires an extended release tablet that performs within specific parameters, as described in the '286 patent. *Id.* at ¶ 20. Selecting the right combination of excipients is thus important in formulating a budesonide dosage form that can achieve the desired PK properties. *Id.* at ¶ 21.

[4] As used here, "upper GI tract" refers to the stomach and small intestine.

B. COSMO'S PATENTED INVENTION

Plaintiffs invented, and claimed in the '286 patent, an extended release formulation for budesonide including specific excipients and other features that permit budesonide extended release tablets to have certain explicit PK parameters which effectively treat ulcerative colitis. On July 11, 2017, Cosmo filed U.S. Patent Application No. 15/646,585 entitled "Controlling Release and Taste Masking Oral Pharmaceutical Composition" with the USPTO. This application published on October 26, 2017, as U.S. Publication No. 2017/0304209 A1, and on August 21, 2018, the USPTO issued the '286 patent. Cosmo is the assignee and owner of the '286 patent and exclusively licenses it to the Bausch plaintiffs.

The specification of the '286 patent discloses that the extended release budesonide tablets consist of a gastro-resistant film covering a tableted core matrix consisting of 9 mg of budesonide, hydroxypropyl cellulose and magnesium stearate. Byrn Decl. ¶25. Several claims of the '286 patent are directed to embodiments that include a starch or starch derivative as part of the core matrix. *See e.g.,* '286 patent at claims 4, 16; Byrn Decl. ¶ 26.

The novel budesonide extended release formulation of the '286 patent is designed to treat ulcerative colitis by releasing the drug specifically in the colon, including the distal colon, thereby achieving a specific oral bioavailability also known as area under the curve ($AUC_{0\text{-}infinity}$) and peak concentration (C_{max}). For example, independent claim 1 of the '286 patent recites that "the oral dosage form provides an $AUC_{0\text{-}infinity}$ . . . of about 16431.2 ± 10519.8 (pg)x(h)/mL," and claim 11 recites that "the oral dosage form provide a C_{max} . . . of about 1348.8 ± 958.8 pg/mL." '286 patent at claim 1. These properties are important to the effective administration of budesonide and are produced by Defendants' Accused Product.

C. UCERIS®

Uceris® is an anti-inflammatory medication that is prescribed to treat symptoms of ulcerative colitis, which was approved by the U.S. Food and Drug Administration ("FDA") on January 14, 2013. Grabowski Decl. ¶ 13. Cosmo invented the proprietary technology platform (MMX Multi Matrix System) which it used to develop the first controlled release formulation that can deliver budesonide throughout the colon. Grabowski Decl. ¶ 14. Cosmo partnered with Bausch to launch the drug in the United States in 2013.

Both Bausch and Cosmo consider Uceris® to be a flagship product. Since its launch in the U.S., licensing fees from Uceris have been a major source of income for Cosmo. Grabowski Decl. ¶ 20. From 2013 through the first half of 2018, Cosmo had cumulative revenues of approximately $435 million, of which Uceris® accounted for approximately $174 million or 40 percent. *Id.* In recent years, as sales of Uceris® grew, its importance for Cosmo's financial health increased as well. In 2016, licensing fees from Uceris® constituted 47.1 percent of Cosmo's overall revenues. *Id.* In 2017, Uceris® contributed 38.2 percent to Cosmo's total revenues. *Id.*

Uceris® is one of the [redacted] high performing drugs for Cosmo, [redacted]. *Id.* at ¶ 21. However due to drastically diminished revenues from [redacted] due to generic entry, Cosmo is now even more reliant on sales of Uceris®. *Id.*

D. DEFENDANTS' ACCUSED PRODUCT

Defendants' Accused Product is a generic version of and direct substitute for Uceris®. Defendants' product label for "budesonide extended-release" describes the Accused Product as a "delayed and extended-release tablet" containing 9 mg of budesonide that "is enteric coated to protect [against] dissolution in gastric juice." Actavis Label at 1. The product label also lists excipients including hydroxypropyl cellulose, magnesium stearate, and sodium starch glycolate,

a starch derivative. Actavis Label at 7, (Section 12.1). The product label also recites the Accused Product's PK properties, including a peak plasma concentration (C_{max}) of 1.35 ± 0.96 ng/mL with area under the plasma concentration time curve (AUC) of approximately 16.43 ± 10.52 ng·hr/mL. *Id.*, "Absorption".

IV. ARGUMENT

The at-risk launch of Defendants' Accused Product only six weeks ago has already caused severe harm to Plaintiffs. A temporary restraining order and preliminary injunction are necessary to restore the *status quo ante* and prevent the harm from becoming irreparable.

A. LEGAL STANDARD

"Federal Circuit law provides the standard for granting an application for a preliminary injunction of patent infringement." *Research Found. Of State Univ. of N.Y. v. Mylan Pharms., Inc.*, 723 F. Supp. 2d 638, 646 (D. Del. 2010) (Stark, M.J.) (*citing Hybridtech, Inc. v. Abbott Labs*, 849 F.2d 1446, 1451 n.12 (Fed. Cir. 1988); *M/A-Com Tech. Solutions Holdings, Inc. v. Laird Techs., Inc.*, 2014 U.S. Dist. LEXIS 86661 (June 16, 2014) (same). '"A plaintiff seeking a preliminary injunction must establish [1] that he is likely to succeed on the merits, [2] that he is likely to suffer irreparable harm in the absence of preliminary relief, [3] that the balance of equities tips in his favor, and [4] that an injunction is in the public interest.'" *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1375-76 (Fed. Cir. 2009) (*quoting Winter v. Natural Res. Def. Council, Inc.*, 555 U.S. 7 (2008)). A request for a temporary restraining order is governed by the same standards that govern the issuance of a preliminary injunction. *See NutriSweet Co. v. Vit-Mar Enterprises, Inc.*, 112 F.3d 689, 693 (3d Cir. 1997); *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 2011 WL 1980610, at *1 (D. Del. May 20, 2010). Each of these four factors weighs in favor of granting Plaintiffs' request for a temporary restraining order and a preliminary injunction

B. PLAINTIFFS ARE LIKELY TO SUCCEED ON THE MERITS

It is probable that Plaintiffs will succeed on the merits of their infringement claim because (1) Defendants are likely infringing one or more claims of the patent-in-suit and (2) at least one of those infringed claims will withstand any validity challenge Defendants may present. *Astrazeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1050 (Fed. Cir. 2010); *In re Cyclobenzaprine*, 2011 WL 1980610 (granting temporary restraining order to enjoin Mylan's at-risk launch of generic versions of the plaintiffs' extended-release cyclobenzaprine products).

1. Infringement

Plaintiffs are likely to prove that Defendants' Accused Product infringes at least claims 6 and 16 of the '286 patent. An infringement analysis involves a two-step process. "The first step is determining the meaning and scope of the patent claims asserted to be infringed. The second step is comparing the properly construed claims to the [process] accused of infringing." *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 237 F.3d 1359, 1363 (Fed. Cir. 2001).

a. Claim Construction

In construing the claims of a patent, a court should normally give the terms in the claims "their ordinary and customary meaning" as understood by "a person of ordinary skill in the art in question." *Phillips v. AWH Corp*., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005). Here, a person with an ordinary level of skill in the art to which the '286 patent pertains would have a degree in chemistry, pharmaceutical chemistry, pharmacy, medicine, clinical pharmacology, pharmacokinetics, or another pharmaceutical science-related field, and at least three years of experience in designing, developing, evaluating, and/or testing pharmaceutical formulations. Byrn Decl. ¶ 39.

Here, the terms of claims 6 and 16 of the '286 patent would be readily understandable to a person of ordinary skill in the art in accordance with their ordinary and customary meaning. Byrn Decl. ¶ 41.

b. Infringement of Claims 6 and 16

As noted by the claim chart in the Byrn Declaration, each of the elements of claims 6 and 16 are present in the Accused Product. Byrn Decl. ¶¶ 45-46. Claim 6 depends from claim 4, which depends from claim 1; claim 16 depends from claim 14, which depends from claim 11. The Accused Product satisfies every element of claims 1 and 11. The Accused Product satisfies the first element of claims 1 and 11 because it "consist[s] essentially of (1) a tableted core, and (2) a gastro-resistant film on said tableted core." Byrn Decl. ¶ 48 (citing Actavis Label at 7-8). The Accused Product further satisfies the first clause of claims 1 and 11 because the tableted core of the Accused Product consists of a matrix comprising 9 mg of budesonide, hydroxypropyl cellulose, and magnesium stearate. Byrn Decl. ¶ 49 (citing Actavis Label at 2, 7, 8). The Accused Product satisfies the second "wherein" clause of claim 1 because, following oral administration of the Accused Product to a human, the oral dosage form provides an $AUC_{0\text{-}inf}$ of budesonide in said human of about 16431.2 ± 10519.8 (pg)(hr)/ml. Byrn Decl. ¶ 50 (citing Actavis Label at 8).[5] The Accused Product satisfies the second "wherein" clause of claim 11 because, following oral administration of the Accused product to a human, the oral dosage form provides a C_{max} of said budesonide in said human of about 1348.8 ± 958.8 pg/mL. Byrn Decl. ¶

[5] Dr. Byrn explains that the AUC reported in the Actavis Label, 16.43 ± 10.52 ng·hr/mL, is an alternative expression for 16430 ± 10520 (pg)(hr)/ml, which is the same as 16431.2 ± 10519.8 (pg)(hr)/ml but reported at fewer significant figures. Byrn Decl. ¶ 50.

51 (citing Actavis Label at 8).[6] The Accused Product satisfies the final "wherein" clause of claims 1 and 11 because it is in the form of a tablet and provides extended release of budesonide in the colon of said human effective to treat ulcerative colitis in said human. Byrn Decl. ¶ 52 (citing Actavis Label at 1, 7).

The Accused Product also satisfies the additional limitation that claims 4 and 14 impose because the matrix of the Accused Product comprises magnesium stearate and sodium starch glycolate, which is a "starch or starch derivative." Byrn Decl. ¶ 53. Finally, the Accused product satisfies the additional limitation that claims 6 and 16 impose since the matrix of the Accused Product comprises sodium starch glycolate which is a starch derivative as recited by the claim. Byrn Decl. ¶ 54. In sum, the Accused Product meets each and every limitation of claims 6 and 16 of the '286 patent and therefore infringes those claims. *See* Byrn ¶ 55.

2. Validity

A patent is entitled to a presumption of validity, which may only be overcome by clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011). This presumption applies through all stages of litigation including "during preliminary injunction proceedings." *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1377 (Fed. Cir. 2009). Because the '286 patent issued after Defendants received approval from the FDA for the Accused Product, Defendants did not serve a Paragraph IV notice with respect to the '286 patent. Unless Defendants can identify clear and convincing evidence of invalidity, the very existence of the asserted patents satisfies Plaintiffs' burden on the validity issue. *Canon Computer Sys., Inc. v. Nu-Kote Int'l, Inc.*, 134 F.3d 1085, 1088 (Fed. Cir. 1998).

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[6] Dr. Bryn explains that the C_{max} reported in the Actavis Label, 1.35 ± 0.96 ng/mL, is an alternative expression for 1350 ± 960 pg/mL, which is the same as 1348.8 ± 958.8 pg/mL but reported at fewer significant figures. Byrn Decl. ¶ 51.

C. PLAINTIFFS WILL SUFFER IRREPARABLE HARM IN THE ABSENCE OF INJUNCTIVE RELIEF

Irreparable harm is established when a plaintiff is unlikely to be made whole by an award of monetary damages or some other legal remedy at a later date, in the ordinary course of litigation. *See Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 726 F.3d 1296, 1304 (Fed. Cir. 2013) (noting that "[p]rice erosion, loss of goodwill, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm."); *see also In re Cyclobenzaprine*, 2011 WL 1980610, at * 3 (finding that "there is a likelihood of irreparable harm for the name brand manufacturer" in every case where a generic threatens to enter the marketplace). Indeed, the patent statute expressly "provides injunctive relief to preserve the legal interests of the parties against future infringement which may have market effects never fully compensable in money." *Sanofi-Synthelabo v. Apotex Inc.*, 488 F. Supp. 2d 317, 342 (S.D.N.Y. 2006), *aff'd* 470 F.3d 1368, 1382-83 (Fed. Cir. 2006).

If Defendants are not enjoined from selling their infringing product, then Plaintiffs will be harmed in ways that can never be fully calculated or remedied through monetary damages. Due to Defendants' at-risk launch of the Accused Product, Plaintiffs have already started to see an immediate and ***real*** harm to their market position. As described more fully in the accompanying declaration of Dr. Henry Grabowski, Defendants' continued infringing sales will at least (1) irrevocably diminish Plaintiffs' market position and cause permanent price erosion; (2) [redacted]; (3) inhibit Cosmo and Bausch's ability to fund, develop and bring new drugs to market; and (4) irrevocably damage Plaintiffs' goodwill with its customers. Under these circumstances, an injunction preventing Defendants from continued sales of the Accused Product (at least until a trial on the merits is completed) is appropriate and necessary.

1. Irrevocable Loss of Market Share and Permanent Price Erosion

Prior to Defendants' launch of their Accused Product, Plaintiffs' patented Uceris® product was the only extended release budesonide tablet on the market, with highly successful yearly sales generating over $134 million dollars in revenue as of FY 2017. Grabowski Decl. ¶ 19. Uceris® net sales grew from $66.3 million since its launch in 2013 to $134.0 million in 2017. *Id.* at ¶19. Figures for the first two quarters of 2018 suggest that 2018 sales of Uceris® could have exceeded its sales in 2017 but for the at risk launch of the Accused Product. *Id.* This projected growth has been and will be severely stunted by Defendants' launch of their infringing Accused Product. *Id.* Data for the first five weeks since the launch of the Accused Product indicate a substantial impact on Uceris® prescriptions. Grabowski Decl. ¶30. During this period, the number of Uceris® prescriptions declined from an average of 2,023 prescriptions per week (over the ten weeks preceding the generic entry) to 1,400 prescriptions per week. *Id.*

Monetary damages will not be enough to compensate Plaintiffs' losses as they cannot compensate for the lost growth of the Uceris® sales or loss of market share. *Bio-Tech. Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1566 (Fed. Cir. 1996) (lost product revenue upon entry of an infringing product may evidence irreparable harm). And these damages cannot be recouped.

In addition to an irreparable decrease in market share, continued sales of Defendants' Accused Product will cause permanent (and incalculable) price erosion, due to market pressures. As a result of Actavis' launch of its Accused Product, Bausch launched a lower-priced authorized generic version of Uceris® which has accounted for approximately [redacted] generic sales during the initial five-week period. Grabowski ¶ 33. The launch of authorized generics is a common strategy employed by branded companies when faced with generic entry. *Id.* [redacted]

[redacted]

[redacted] Grabowski ¶ 31. Uceris® will continue to lose sales volume and market share absent an injunction. *Id.* at ¶ 32.

Entry by a generic drug inevitably causes a precipitous loss in sales, prescriptions, profits, and market share of the reference branded drug. *Id.* at ¶ 22. When a generic product is considered to be therapeutically equivalent to the branded product (as is Defendants' Accused Product), the substitution for the cheaper generic is almost always automatic at the pharmacy level, unless the prescribing physician indicates otherwise. Grabowski Decl. ¶ 22-24. At the same time, Pharmacy Benefit Managers ("PBMs") and public and private Third-Party Payers ("TPPs"), such as Medicare plans and private insurance plans, strongly encourage patient substitution to cheaper generic products by utilizing tiered drug formularies[7] or formulary restrictions. *Id*. at ¶ 23.

Furthermore, the longer Defendants stay on the market with their infringing Accused Product, the more likely it is that TPPs and PBMs will remove Uceris® from their formularies and that pharmacies will automatically substitute Defendants' Accused Product for Uceris®. Grabowski Decl. ¶ 36; *Abbott*, 500 F. Supp. 2d at 844 (removal from formularies weighed in favor of injunction).

[redacted]

[redacted]. Grabowski Decl. ¶ 33. [redacted]

[7] Drug formularies are lists of approved drugs that will have their costs reimbursed by the TPP to the patient and pharmacy when prescribed for a given medical problem. A prevalent type of formulary currently employed is a three-tier system, wherein drugs in the same therapeutic class are grouped into three tiers. Generic drugs are typically on Tier 1 with the lowest copayments by patients; preferred branded drugs are on Tier 2 with higher copayments; and non-preferred branded drugs are on Tier 3 with the highest copayments. Grabowski Decl. ¶ 23; *Abbott Labs. v. Sandoz, Inc.*, 500 F. Supp. 2d 807, 844 (N.D. Ill. 2007).

[redacted] *Id.* Indeed, even if Plaintiffs later succeed on the merits of their patent infringement lawsuits, TPPs and PBMs will not accept significant price increases after having enjoyed lower, generic drug prices for an extended period of time. *Id.* at ¶ 35; *see also Sanofi-Synthelabo*, 470 F.3d at 1382-83 (finding irreparable harm where the patentee asserted that it would be "nearly impossible to restore [the branded drug] to its pre-launch price since the generic product entered the market"); *Polymer Techs., Inc. v. Bridwell*, 103 F.3d 970, 975-76 (Fed. Cir. 1996) (finding no rebuttal of the presumption of irreparable harm because requiring purchasers to pay higher prices after paying lower prices to infringers "is not a reliable business option.").

Currently, Uceris® has a preferred formulary placement on almost 40 percent of commercial health insurance plans (by lives covered). Grabowski Decl. ¶ 36. Among the top ten commercial health insurance plans (excluding Kaiser Permanente), only one plan does not provide prescription drug formulary coverage for Uceris®, and only two plans impose formulary restrictions (prior authorization or quantity limits) on Uceris®. *Id.* [redacted], it is likely that these TPPs would move Uceris® to a formulary tier requiring higher co-payments or would impose other formulary restrictions on Uceris®. *Id.*

The process for inclusion in such formularies is difficult and time-consuming, requiring complicated contract negotiations. Because the negotiation process between TPPs and pharmaceutical companies takes time, the longer the Accused Product remains on the market, the more likely it is that other TPPs and PBMs will [redacted] extract [redacted] rebates for Uceris®. Grabowski Decl. ¶ 35. Absent an immediate injunction, there is no assurance that Uceris®

would be restored to its current formulary position even if Defendants' Accused Product were subsequently removed from the market. *Id.* For this reason, if the Accused Product is not enjoined shortly, there will be continued price erosion for Uceris®, and this price erosion may be difficult to reverse in the future.

2. [redacted] and Goodwill

Bausch is the industry leader in the treatment of GI conditions and has an extensive sales force marketing its products to gastroenterologists, hepatologists, and primary care physicians, among others. Grabowski Decl. ¶ 45. Uceris® is the number [redacted] product for Salix and until Actavis' recent launch of its Accused Product, Uceris® was the product that Bausch's GI-dedicated sales force [redacted] *Id.* If Defendants are not enjoined, [redacted], particularly since any marketing efforts would only serve to increase prescriptions for the generic version of Uceris® that will be filled by Defendants' infringing Accused Product. As a result, Bausch may [redacted]. Grabowski Decl. ¶¶ 45, 59-62. The harm from this [redacted] may be greatly minimized, if not altogether avoided, if sales of the Accused Product are enjoined shortly.

Once Bausch's marketing efforts cease, so too will the potential product growth and the continued generation of goodwill for Uceris® amongst physicians. The loss of benefits from these relationships that would occur [redacted] would be difficult to quantify to a reasonable degree of economic certainty. *Id.* Further, Salix is likely to experience reputational loss from its curtailment of promotional activity for Uceris®, [redacted] as

[redacted]. *Id.* at ¶ 61. This reputational loss will be difficult to quantify to a reasonable degree of economic certainty. *Id.* Even if Defendants are later enjoined after Plaintiffs succeed at trial, it will be difficult and time-consuming for Bausch to [redacted] and will not be able to recover this lost momentum and restore Uceris® sales and growth to what it would have been prior to Defendants' sales of their infringing product. Grabowski Decl. ¶ 48; *see also Sanofi-Synthelabo*, 470 F.3d at 1383 (listing "loss of goodwill, the potential reduction in work force, and the discontinuation of clinical trials" as factors that establish irreparable harm); *Purdue Pharma*, 237 F.3d at 1368; *Polymer Techs.*, 103 F.3d at 975-76 (finding irreparable harm, in part, because "[c]ustomers may have established relationships with infringers").

3. Lost Research and Development and Lost Market Opportunities

The loss of revenue from Cosmo's highly profitable flagship product would irreparably harm its ongoing development and licensing of new drug candidates and its ability to bring beneficial therapies to patients in need. Grabowski Decl. ¶¶ 41-43. Pharmaceutical R&D is a complicated, time-consuming, and extremely costly endeavor without any guarantee of success. *Id.* at ¶ 41. To increase the likelihood of success in an R&D program, an innovator company must explore a variety of research initiatives and projects, as the success of any single project is uncertain. *Id.* Sales generated by Uceris® constitute an important source of financing for pharmaceutical R&D. *Id*. at ¶ 42. The dramatic reduction in Uceris® revenues resulting from sales of the Accused Product would significantly hinder both Cosmo's and Bausch's ability to reinvest in R&D and develop new products.

Cosmo is a research-intensive company that focuses on the development of novel treatments for colon diseases. *Id*. at ¶ 43. In addition to Uceris®, Cosmo has a pipeline of drugs in different stages of preclinical and clinical development. *Id.* As is typical for a pharmaceutical

development company, Cosmo invests a large percent of its revenue into R&D. *Id.* Given the relationship between sales and the R&D budget, the continued decline in Uceris® sales due to the at-risk launch of the Accused Product would deprive Cosmo of a large portion of its R&D financing and is likely to cause a reduction in Cosmo's R&D efforts. *Id.* Curtailing R&D activities may result in a substantial decline of future profitability if such R&D efforts were to lead to the development of drugs approved for marketing. *Id.* Even postponing R&D is costly, as it may result in the loss of the first-to-market status for innovator products. *Id.*

Consequently, if Defendants are allowed to keep the infringing Accused Product on the market, Cosmo and Bausch will be forced to substantially decrease their R&D activities. The harm resulting from this decrease is difficult to quantify as it is hard to measure its impact on Plaintiffs and the patients who could have benefitted from the research findings.

D. THE BALANCE OF THE HARDSHIPS FAVORS THE ISSUANCE OF INJUNCTIVE RELIEF

Plaintiffs stand to suffer much greater hardship than Defendants if a TRO and preliminary injunction are wrongfully withheld. Defendants' infringement has already caused ***real***, not imaginary or speculative, severe harm which if not stopped will be irreparable. In evaluating the balance of hardships, the "district court must balance the harm that will occur to the moving party from the denial of the preliminary injunction with the harm that the non-moving party will incur if the injunction is granted." *Hybritech*, 849 F. 2d at 1457.

As discussed above, Uceris® is the flagship product of Cosmo's limited number of pharmaceutical products. Plaintiffs have expended significant resources to research, develop, patent, and promote Uceris® and would lose the value of its investment if Defendants were permitted to prematurely remain on the market with their infringing product. In contrast, the cost to Defendants resulting from an injunction is likely to be much smaller than the corresponding

lost profits for Plaintiffs. Grabowski Decl. ¶ 65. Accordingly, based on a comparison between Defendants' and Cosmo's size and revenue alone, it is apparent that Defendants are better positioned to withstand any near-term harm associated with an injunction. *Id.* at ¶¶ 65-66.

In addition to the incalculable loss of market position and price erosion to their flagship product, [redacted], curtail their research and development spending, and destroy the goodwill that Plaintiffs have established. Grabowski Decl. ¶ 64. This loss of value, together with the other hallmark signs of irreparable harm discussed above, weighs heavily in favor of a TRO and a preliminary injunction. *See In re Cyclobenzaprine*, 2011 WL 1980610 at *4. By contrast, assuming *arguendo* that Defendants do not infringe, an injunction would cost nothing more than a temporary halt to their sales which can be easily compensated for and guaranteed by an injunction bond. Grabowski Decl. ¶ 65. Defendants have only recently entered the market and would bear little to no hardship if enjoined while the Court decides this case on the merits. *Id*. Indeed, courts have found minimal hardship to an alleged infringer who is either not on the market yet or is in the early stages of marketing its product. *See PPG Indus. Inc. v. Guardian Indus. Corp*., 75 F.3d 1558, 1567 (Fed. Cir. 1996).

Here, Defendants made a calculated decision to launch their product at risk during the appeal from the ANDA Litigation, and further likely had knowledge of the application that issued as '286 patent prior to launching their product. Nonetheless, Defendants took a gamble and launched their infringing product prior to the final determination on the merits. Although Defendants have quickly captured market share, they have been on the market for only about 6 weeks. Thus, they will suffer minimal losses if a legally-sanctioned market entry, if any, is delayed until this Court makes a decision on the merits. *See Sanofi-Synthelabo*, 470 F.3d at 1383 (concluding that district court did not clearly err in finding that challenger's harms were almost

entirely preventable and were the result of its own calculated risk to launch its product pre-judgment); *Pfizer*, 429 F.3d at 1382 ("Simply put, an alleged infringer's loss of market share and customer relationships, without more, does not rise to the level necessary to overcome the loss of exclusivity experienced by a patent owner due to infringing conduct.") As such, Defendants should not be allowed to complain about any resulting harm from an injunction.

E. THE PUBLIC INTEREST FAVORS INJUNCTIVE RELIEF

Consideration of the effect of Plaintiffs' requested relief on the public's interest weighs in favor of granting a preliminary injunction. In patent infringement cases, the analysis of this factor focuses on whether the grant of injunctive relief would injure some "critical public interest." *Hybritech, Inc.*, 849 F.2d at 1458. "[I]t is generally in the public interest to uphold patent rights." *Broadcom Corp. v. Qualcomm Inc.*, 543 F.3d 683, 704 (Fed. Cir. 2008). Courts have long acknowledged the importance of the patent system in encouraging innovative drug companies to continue costly development and research efforts. *Sanofi-Synthelabo*, 470 F.3d 1368, 1383 (Fed. Cir. 2006); *Abbott Labs v. Sandoz, Inc.*, 544 F.3d 1341, 1362-63 (Fed. Cir. 2008). Plaintiffs invest heavily in research and development of new drugs. Grabowski Decl. ¶¶ 54-58. Cosmo's ability to sustain this practice would be seriously eroded without assurance that its research will be protected under the patent system. *Id.* at ¶¶ 54, 67.

In evaluating the public interest factor, courts must consider the right to exclude, which is "the heart of the patent grant." *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1341 (Fed. Cir. 2012).

In this case, the benefits of the patent system encourage Plaintiffs like Cosmo to invest the significant resources necessary to research and develop new products. Grabowski Decl. ¶ 70. There is a strong public interest in encouraging investment by pharmaceutical companies through the issuance and enforcement of patents rights. *See Sanofi-Synthelabo*, 470 F.3d at 1383-84

(acknowledging the "public interest in encouraging investment in drug development and protecting the exclusionary rights conveyed in valid pharmaceutical patents").

No public interest factor outweighs encouraging this type of investment in drug development. Furthermore, although Defendants' product will result in a lower market price for the product, lower prices do not justify patent infringement. *Payless Shoesource, Inc.v. Reebok Int'l, Ltd.*, 998 F.2d 985, 991 (Fed. Cir. 1993) ("selling a lower priced product does not justify infringing a patent"); *accord Pfizer*, 429 F.3d at 1382. Accordingly, the public interest favors the issuance of a preliminary injunction in this case.

V. CONCLUSION

For the foregoing reasons, Plaintiffs request that the Court enter an Order enjoining Defendants from further commercially manufacturing, using, offering to sell, or selling within the United States or importing into the United States the Accused Product.

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