IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICALS U.S.A., INC., Plaintiff, v. DR. REDDY'S LABORATORIES, LTD. and DR. REDDY'S LABORATORIES, INC. Defendants.	Civil Action No. _____

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Takeda Pharmaceuticals U.S.A., Inc. ("Takeda") files this Complaint for patent infringement against Defendants Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc. (collectively "DRL" or "Defendants") and, in support thereof, alleges as follows.

NATURE OF THE ACTION

1. This is an action for patent infringement under the Food and Drug and Patent Laws of the United States, U.S.C. Titles 21 and 35 respectively, arising from DRL's submission of Abbreviated New Drug Application ("ANDA") No. 209876 (the "DRL ANDA") to the United States Food and Drug Administration ("FDA"), seeking approval to sell commercially a generic version of the drug product Colcrys® (colchicine, USP) (the "ANDA Product") prior to the expiration of United States Patent Nos. 7,906,519; 7,935,731; 8,093,298; 7,964,648; 8,093,297; 7,619,004; 7,601,758; 7,820,681; 7,915,269; 7,964,647; 7,981,938; 8,093,296; 8,097,655; 8,415,395; 8,415,396; 8,440,721; and 8,440,722, which cover, *inter alia*, methods of using colchicine for treating and preventing gout flares and treating Familial Mediterranean Fever.

THE PARTIES

2. Takeda Pharmaceuticals U.S.A., Inc. is a Delaware corporation with its principal place of business at One Takeda Parkway, Deerfield, IL 60015. Takeda holds all right, title and interest in each patent asserted in this action.

3. On information and belief, Defendant Dr. Reddy's Laboratories, Ltd. ("DRL Ltd.") is a company organized and existing under the laws of India, having a principal place of business at 8-2-337, Road No. 3, Banjara Hills, Hyderabad, Andhra Pradesh 500034, India.

4. Upon information and belief, Defendant Dr. Reddy's Laboratories, Inc. ("DRL Inc.") is a wholly owned subsidiary of Dr. Reddy's Laboratories, Ltd., and is a company organized and existing under the laws of the State of New Jersey, having a principal place of business at 107 College Road East, Princeton, New Jersey 08540.

5. Upon information and belief, DRL Inc. is an agent or affiliate of DRL Ltd. and is acting as the agent of DRL Ltd. with respect to Abbreviated New Drug Application ("ANDA") No. 209876.

6. On information and belief, DRL Inc. markets, distributes, sells and/or offers for sale generic drugs throughout the United States and in Delaware at the direction of, under the control of, in concert with, and for the direct benefit of DRL Ltd.

7. Upon information and belief, DRL Inc. assisted in the preparation and submission of ANDA No. 209876, which was done at the direction of, under the control of, in concert with, and for the direct benefit of DRL Ltd.

8. Upon information and belief, following any FDA approval of ANDA No. 209876, DRL Ltd. and DRL Inc. will act in concert to market, distribute, offer for sale, and sell DRL's ANDA Product throughout the United States and within Delaware.

JURISDICTION AND VENUE

9. This action for patent infringement arises under 35 U.S.C. § 271.

10. This Court has subject matter jurisdiction over this matter pursuant to 28 U.S.C. §§ 1331 and 1338(a), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

11. This Court has personal jurisdiction over DRL Ltd. and DRL Inc. under the laws of Delaware, 10 Del. C. § 3104(c), and/or Fed. R. Civ. P. 4(k)(2).

12. Venue is proper in this District under 28 U.S.C. § 1400(b) and/or 28 U.S.C. § 1391(b) and/or (c).

13. By correspondence dated January 5, 2018, Counsel for DRL Ltd. and DRL Inc. stated: "For purposes of this matter only" DRL Ltd. and DRL Inc. "will consent to personal jurisdiction and venue in Delaware."

STATEMENT OF FACTS RELEVANT TO ALL COUNTS

14. Takeda is the holder of New Drug Application ("NDA") Nos. 22-351, 22-352, and 22-353, pursuant to which the FDA granted approval in 2009 for the commercial manufacturing, marketing, sale, and use of Colcrys® (colchicine, USP) tablets, 0.6 mg, pursuant to section 505(b) of the Federal Food Drug and Cosmetics Act ("FFDCA"), 21 U.S.C. § 355(b).

15. Colcrys® is primarily used to prevent and treat gout flares. Gout is a type of severe arthritis typically characterized by extremely painful "flares" (severe and sudden attacks of pain, redness, inflammation, and tenderness in joints) resulting from a build-up of uric acid. Colcrys® and Takeda's authorized generic of Colcrys® are the only oral single-active-ingredient colchicine products approved by the FDA for the treatment and prevention of gout flares.

16. Colcrys® is also used to treat Familial Mediterranean Fever ("FMF"). FMF is a rare, autosomal recessive, auto-inflammatory disease characterized by recurrent and/or chronic

inflammation. Colcrys® and Takeda's authorized generic of Colcrys® are the only single-active-ingredient oral colchicine products currently on the market to treat FMF.

17. As part of the FDA approval for Colcrys®, Takeda received Orphan Drug exclusivity, which expired July 29, 2016.

18. At the time the FDA granted approval to Colcrys® in 2009, the NDA holder was Takeda's predecessor-in-interest, Mutual Pharmaceutical Company, Inc. ("Mutual"). Mutual conducted groundbreaking research, discovering important new information about colchicine, including previously unknown information concerning safety and efficacy, tolerability, dangerous side effects, and interactions with other medicines and substances.

19. Before Colcrys®, no oral single-ingredient colchicine had been reviewed by the FDA for safety and efficacy. The lack of FDA-reviewed data regarding oral single-ingredient colchicine was particularly troublesome because colchicine is potentially toxic. Before Mutual introduced Colcrys®, oral colchicine had been associated with more than 160 deaths. Accordingly, to support the safe and effective use of an oral single-ingredient colchicine product, Mutual developed its own formulation and studied the effects of that formulation in human subjects.

20. One of Mutual's clinical studies, the Acute Gout Flare Receiving Colchicine Evaluation ("AGREE") trial, provided important new information on the optimal dose of colchicine for treatment of gout flares. Traditionally, oral colchicine had been used for the treatment of gout flares by administering an initial dose of one to two 0.6 mg tablets at the onset of the flare, followed by additional doses every one to two hours until either the pain subsided or "nausea, vomiting, or diarrhea" developed. Many patients following this regimen would take a

total dose of up to 8 mg of colchicine, which frequently led to toxicity-related side effects such as diarrhea or vomiting.

21. The AGREE trial completely upended the conventional wisdom. The trial was a double-blind, placebo-controlled, multicenter, dose-comparison study involving 575 trial participants. It compared the effects of the "traditional" dose described above to a lower dose of just 1.8 mg total of colchicine, administered as 1.2 mg colchicine followed by 0.6 mg 1 hour later. The AGREE trial proved that the lower-dose regimen is just as effective as the traditional higher-dose regimen but without the serious adverse events of the higher dose. Based on Mutual's trial, the FDA approved Mutual's colchicine product with the low-dose regimen as safe and effective for the treatment of gout flares. The Colcrys® low-dose regimen is recited in the FDA-approved product label attached as Exhibit A.

22. In 2012, the American College of Rheumatology ("ACR") issued guidelines for management of gout. The ACR guidelines adopt Takeda's low-dose regimen. The ACR recommends treating an acute gout flare by using a loading dose of 1.2 mg of colchicine, followed by 0.6 mg 1 hour later, and then, 12 hours later, resuming 0.6 mg prophylactic dosing once or twice daily, unless dose adjustment is necessary. The ACR recommendation remains the standard of care for the use of colchicine to treat acute gout flares. Part II of the ACR guidelines, addressing therapy and prophylaxis of acute gouty arthritis, is attached as Exhibit B. *See* Ex. B at 1453.

23. Mutual also conducted multiple studies regarding potential adverse drug interactions involving colchicine. Mutual researched numerous drug interactions that could result in unsafe levels of colchicine and even death. Mutual discovered, for example, that co-administering colchicine with clarithromycin could increase colchicine blood levels by nearly

230%, creating a risk of toxicity. Mutual identified potentially dangerous interactions between colchicine and several other drugs, and it recommended colchicine dosing reductions to reduce the risk of an adverse reaction when colchicine is administered concomitantly with such other drugs. This dose adjustment information is currently included in the approved labeling for Colcrys®, which specifies appropriate dose adjustments when Colcrys® is co-administered with ketoconazole, verapamil, ritonavir, clarithromycin, and other drugs. *See, e.g.*, Ex. A at Table 1; *see also* Ex. B at 1453 (ACR Guidelines recommending dose adjustments in Colcrys labeling).

TAKEDA'S COLCRYS® PATENTS

24. Takeda is the lawful owner of all right, title, and interest in and to the following United States patents, including the right to sue and to recover for infringement thereof, which contain one or more claims covering methods of using Colcrys®.

A. United Sates Patent Number 7,906,519 ("the '519 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit C and incorporated herein by reference as though set forth in full, which was duly and legally issued March 15, 2011, naming Matthew Davis as the inventor.

B. United States Patent Number 7,935,731 ("the '731 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit D and incorporated herein by reference as though set forth in full, which was duly and legally issued May 3, 2011, naming Matthew Davis as the inventor.

C. United States Patent Number 8,093,298 ("the '298 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit E and

incorporated herein by reference as though set forth in full, which was duly and legally issued January 10, 2012, naming Matthew Davis as the inventor.

D. United States Patent Number 7,964,648 ("the '648 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit F and incorporated herein by reference as though set forth in full, which was duly and legally issued June 21, 2011, naming Matthew Davis as the inventor.

E. United States Patent Number 8,093,297 ("the '297 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit G and incorporated herein by reference as though set forth in full, which was duly and legally issued January 10, 2012, naming Matthew Davis as the inventor.

F. United States Patent Number 7,619,004 ("the '004 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit H and incorporated herein by reference as though set forth in full, which was duly and legally issued November 17, 2009, naming Matthew Davis as the inventor.

G. United States Patent Number 7,601,758 ("the '758 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS IN THE TREATMENT OF GOUT FLARES," a copy of which is attached hereto as Exhibit I and incorporated herein by reference as though set forth in full, which was duly and legally issued October 13, 2009, naming Matthew Davis as the inventor.

H. United States Patent Number 7,820,681 ("the '681 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit J and incorporated herein by reference as though set forth in full, which was duly and legally issued October 26, 2010, naming Matthew Davis as the inventor.

I. United States Patent Number 7,915,269 ("the '269 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit K and incorporated herein by reference as though set forth in full, which was duly and legally issued March 29, 2011, naming Matthew Davis as the inventor.

J. United States Patent Number 7,964,647 ("the '647 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as Exhibit L and incorporated herein by reference as though set forth in full, which was duly and legally issued June 21, 2011, naming Matthew Davis as the inventor.

K. United States Patent Number 7,981,938 ("the '938 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as Exhibit M and incorporated herein by reference as though set forth in full, which was duly and legally issued July 19, 2011, naming Matthew Davis as the inventor.

L. United States Patent Number 8,093,296 ("the '296 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit N and incorporated herein by reference as though set forth in full, which was duly and legally issued January 10, 2012, naming Matthew Davis as the inventor.

M. United States Patent Number 8,097,655 ("the '655 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit O and incorporated herein by reference as though set forth in full, which was duly and legally issued January 17, 2012, naming Matthew Davis as the inventor.

N. United States Patent Number 8,415,395 ("the '395 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as Exhibit P and incorporated herein by reference as though set forth in full, which was duly and legally issued April 9, 2013, naming Matthew Davis and Hengsheng Feng as inventors.

O. United States Patent Number 8,415,396 ("the '396 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as Exhibit Q and incorporated herein by reference as though set forth in full, which was duly and legally issued April 9, 2013, naming Matthew Davis and Hengsheng Feng as inventors.

P. United States Patent Number 8,440,721 ("the '721 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit R and incorporated herein by reference as though set forth in full, which was duly and legally issued May 14, 2013, naming Matthew Davis as the inventor.

Q. United States Patent Number 8,440,722 ("the '722 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit S and incorporated herein by reference as though set forth in full, which was duly and legally issued May 14, 2013, naming Matthew Davis as the inventor.

25. The ’519, ’731, ’298, ’648 and ’297 Patents are collectively referred to herein as the “FMF Patents.”

26. The ’004, ’758, ’681, ’269, ’647, ’648, ’938, ’296, ’297, ’655, ’395, ’396, ’721, and ’722 Patents are collectively referred to herein as the “Gout Patents.” (The ’648 and ’297 patents are both FMF Patents and Gout Patents.)

27. All of the above-listed patents are collectively referred to herein as the “Colcrys® Patents.”

28. The Colcrys® Patents are listed in the FDA’s “Approved Drug Products with Therapeutic Equivalence Evaluations” (commonly referred to as the “Orange Book”) as patents “with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.” 21 U.S.C. § 355(b)(1).

THE GOUT AND FMF MARKETS IN THE UNITED STATES

29. Colcrys® is predominantly used as a medication for treating or preventing gout flares. According to the American College of Rheumatology National Health and Nutrition Examination Survey, as of 2008, 8.3 million people in the United States suffered from gout.

30. On information and belief, the DRL ANDA at issue in this action seeks approval from the FDA to sell generic colchicine tablets solely for the FMF indication, and not for gout. The National Institute of Health Office of Rare Diseases classifies FMF as a “rare disease” with fewer than 200,000 affected individuals in the United States.

31. According to national prescription data from inVentiv Health (formerly Encuity Research), for the fifteen-year period between August 2001 and August 2016, only approximately 32,000 colchicine prescriptions were written for FMF patients in the United States (*i.e.*, only 2,133 prescriptions per year for FMF, compared to 913,000 prescriptions per year for

gout). According to this national prescription data, less than one percent (0.21%) (or approximately 1 in 472) of colchicine prescription were for FMF. And among prescriptions written for FDA-approved uses for colchicine—gout and FMF—approximately 0.23% (or approximately 1 in 449) of the prescriptions were for FMF, while approximately 99.77% of the prescriptions were for gout.

32. On information and belief, DRL intends to manufacture its generic version of Colcrys® in quantities that far exceed the available market for the treatment of FMF in the United States. Upon further information and belief, DRL intends to market its generic version of Colcrys® to prescribers and healthcare practitioners for the treatment and prevention of gout.

PHYSICIAN PRESCRIBING PRACTICES AND PHARMACY DISPENSING PRACTICES

33. Physicians make prescribing decisions for medication based on their knowledge, experience, training, and review of medical literature, including the Physicians' Desk Reference and the package insert or "label" that accompanies a brand drug. Physicians do not generally receive or review generic drug labels. By the time a generic version of a branded drug becomes available, physicians typically have had years of experience prescribing the brand drug, and will follow the same prescribing practices for the generic version. Thus, physicians generally prescribe a generic drug for all of the approved indications associated with the branded drug whether or not that indication appears on the generic label. On information and belief, if DRL markets a generic version of Colcrys® with a label indicating that the drug is approved only for the FMF indication, physicians will nonetheless prescribe colchicine for gout consistent with their previous prescriptions practices for Colcrys®.

34. Physicians typically do not control whether a pharmacist fills a prescription with a brand drug or with any particular generic version. The majority of states allow pharmacists to

substitute generic drugs for brand name drugs so long as the patient approves. Indeed, in fifteen states, substitution of the generic version of a drug is mandatory. *See* 2016 National Association of Boards of Pharmacy (NABP) *Survey of Pharmacy Law* at 71-74 (attached hereto as Exhibit T) (reporting that fifteen states require "mandatory" generic substitution and that forty-nine states permit substitution without permission from the prescriber or purchaser). Even where substitution is not required, pharmacists have an incentive to substitute generic products for brand products because of the lower patient cost and larger pharmacy profit margins associated with generic products. *See*, *e.g.*, Jim Edwards, Moneywatch—CBS News, *How Pharmacists Keep Cash That Could Be Yours on Each Generic Prescription* (May 27, 2011), http://www.cbsnews.com/news/how-pharmacists-keep-cash-that-could-be-yours-on-each-generic-prescription/, a copy of which is attached hereto as Exhibit U. Thus, where a generic version of a brand drug exists, pharmacists regularly will substitute the generic drug for the brand, regardless of whether the generic drug is FDA-approved for the indication for which the brand drug was prescribed.

35. Before 2009, a number of colchicine products were sold in the United States without FDA approval. During that time, physicians would typically write prescriptions for "colchicine" rather than for a particular brand of the drug. Prescription data indicates that many treating physicians have maintained this practice even after unapproved colchicine products were removed from the market and Colcrys® (and its authorized generic) became the only FDA-approved single-ingredient oral colchicine product. Even in states without mandatory substitution laws, a prescription written for "colchicine" rather than Colcrys® will typically be filled with a generic colchicine product if one is available.

36. On information and belief, if DRL markets a generic version of Colcrys® with a label containing only an FMF indication, prescriptions written for "Colcrys®" and "colchicine" for the treatment and/or prevention of gout flares will be filled with DRL's generic colchicine product.

DRL's ACTIONS GIVING RISE TO THIS SUIT

37. DRL submitted ANDA No. 209876 to the FDA seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of 0.6 mg oral colchicine tablets (i.e., DRL's ANDA Product) prior to the expiration of Takeda's patents relating to Colcrys®.

38. On or about December 11, 2017 Takeda received a letter dated December 7, 2017 notifying Takeda of DRL's submission to the FDA of ANDA No. 209876, seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of DRL's ANDA Product to treat FMF and containing a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") with respect to, *inter alia*, the '519, '731, '298, '648, and '297 Patents (hereinafter, the "Paragraph IV Notice Letter"). The Paragraph IV Notice Letter was sent by both DRL Inc. and DRL Ltd. DRL asserted in its Paragraph IV Notice Letter that it is entitled to bring its product to market prior to the expiration of Takeda's '519, '731, '298, '648, and '297 Patents because those patents are invalid, unenforceable, and/or would not be infringed.

39. DRL's Paragraph IV Notice Letter included a detailed statement of the factual and legal basis for the certifications set forth in DRL's ANDA. DRL's Paragraph IV Notice Letter set forth DRL's positions regarding the non-infringement and invalidity of the '519, '731, '298, '648, and '297 Patents.

40. DRL's Paragraph IV Notice Letter also included an offer to the patentee of confidential access pursuant to 21 U.S.C. § 355(G)(5)(C).

41. DRL's Paragraph IV Notice Letter did not state that DRL is seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of its ANDA Product for the treatment or prevention of gout flares. Takeda is informed and believes the DRL has submitted a statement under 35 U.S.C. § 355(j)(2)(A)(viii) ("section viii carve-out") to the FDA with respect to Takeda's Gout Patents.

42. Takeda commenced this action within 45 days of receiving DRL's Paragraph IV Notice Letter.

DRL's INFRINGEMENT OF THE FMF PATENTS

43. Takeda's FDA approved product label for Colcrys® teaches and encourages, *inter alia*, methods of using Colcrys® claimed in the FMF Patents, including the use of colchicine to treat FMF when a patient is or is not taking another substance. *See, e.g.*, Ex. A at Table 1.

44. Under the FFDCA, drug products submitted to the FDA for approval via an ANDA are required to have the same labeling as the reference listed drug, here Colcrys®, except for changes required because of differences approved under a suitability petition (21 U.S.C. § 355(j)(2)(C); 21 C.F.R. § 314.93), because the generic drug product and reference listed drug are produced or distributed by different manufacturers (21 U.S.C. § 355(j)(2)(A)(v); 21 C.F.R. §314.94(a)(8)(iv)), or because the ANDA applicant has made a section viii carve-out for one of the indications on the label of the reference listed drug.

45. The approved labeling for Colcrys® recites the claimed methods of Takeda's FMF Patents. The Colcrys® labeling states that "[c]o-administration of COLCRYS with drugs known to inhibit CYP3A4 and/or P-glycoprotein (P-gp) increases the risk of colchicine-induced toxic effects (Table 1). If patients are taking or have recently completed treatment with drugs listed in Table 1 within the prior 14 days, the dose adjustments are as shown on the table below [see DRUG INTERACTIONS (7)]." *See* Ex. A § 2.4; *see also id.* § 7 ("Table 1 provides

recommendations for strong and moderate CYP3A4 inhibitors and P-gp inhibitors."). Table 1 is reproduced in part below:

Table 1
COLCRYS Dose Adjustment for Co-administration with Interacting Drugs if no Alternative Available[1]

Strong CYP3A4 Inhibitors[2]							
Drug	**Noted or Anticipated Outcome**	**Gout Flares**				**FMF**	
		Prophylaxis of Gout Flares		**Treatment of Gout Flares**			
		Original Intended Dosage	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**
Atazanavir Clarithromycin Darunavir/ Ritonavir[3] Indinavir Itraconazole Ketoconazole Lopinavir/ Ritonavir[3] Nefazodone Nelfinavir Ritonavir Saquinavir Telithromycin Tipranavir/ Ritonavir[3]	Significant increase in colchicine plasma levels[3]; fatal colchicine toxicity has been reported with clarithromycin, a strong CYP3A4 inhibitor. Similarly, significant increase in colchicine plasma levels is anticipated with other strong CYP3A4 inhibitors.	0.6 mg twice a day 0.6 mg once a day	0.3 mg once a day 0.3 mg once every other day	1.2 mg (2 tablets) followed by 0.6 mg (1 tablet) 1 hour later. Dose to be repeated no earlier than 3 days.	0.6 mg (1 tablet) x 1 dose, followed by 0.3 mg (1/2 tablet) 1 hour later. Dose to be repeated no earlier than 3 days.	Maximum daily dose of 1.2 – 2.4 mg	Maximum daily dose of 0.6 mg (may be given as 0.3 mg twice a day)
Moderate CYP3A4 Inhibitors							
Drug	**Noted or Anticipated Outcome**	**Gout Flares**				**FMF**	
		Prophylaxis of Gout Flares		**Treatment of Gout Flares**			
		Original Intended Dosage	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**
Amprenavir[3] Aprepitant Diltiazem Erythromycin Fluconazole Fosamprenavir[3] (pro-drug of Amprenavir) Grapefruit Juice Verapamil	Significant increase in colchicine plasma concentration is anticipated. Neuromuscular toxicity has been reported with diltiazem and verapamil interactions.	0.6 mg twice a day 0.6 mg once a day	0.3 mg twice a day or 0.6 mg once a day 0.3 mg once a day	1.2 mg (2 tablets) followed by 0.6 mg (1 tablet) 1 hour later. Dose to be repeated no earlier than 3 days.	1.2 mg (2 tablets) x 1 dose. Dose to be repeated no earlier than 3 days.	Maximum daily dose of 1.2 – 2.4 mg.	Maximum daily dose of 1.2 mg (may be given as 0.6 mg twice a day)

46. The Colcrys® labeling provides dose adjustments for colchicine when coadministered with ketoconazole, verapamil, ritonavir, clarithromycin, and other drugs. These dose adjustments are disclosed and claimed in Takeda's Patents. For example, claim 1 of the '298 patent recites the following:

> 1. A method of using colchicine for the treatment of Familial Mediterranean Fever in a human adult or child> 12 years of age in need of treatment thereof, said method comprising:
>
> orally administering a reduced colchicine dosage amount to the human adult or child > 12 years of age in need of

> treatment for Familial Mediterranean Fever who is concomitantly receiving administration of clarithromycin within 1 to 2 days of oral administration of colchicine, wherein the reduced colchicine dosage amount is reduced compared to a daily dosage amount to be administered in the absence of concomitant clarithromycin,
>
> wherein the daily dosage amount to be administered in the absence of concomitant clarithromycin is a maximum of 2.4 mg per day, and
>
> wherein the reduced colchicine dosage amount is a maximum of 0.6 mg per day.

See Ex. E, claim 1. The dose adjustment table in the Colcrys® labeling provides that the usual intended dose of colchicine for FMF is a maximum of 2.4 mg. When colchicine is used with a strong CYP3A4 inhibitor such as clarithromycin, the Colcrys® labeling teaches that it should be adjusted from 2.4 mg per day to a reduced colchicine dosage of 0.6 mg per day (which may be given as 0.3 mg twice per day).

47. Accordingly, on information and belief, DRL's labeling for its ANDA Product, like the labeling for Colcrys®, recites methods of using colchicine disclosed and claimed in the FMF Patents.

48. If DRL's ANDA Product is approved by the FDA, DRL will induce others to infringe one or more claims of the FMF Patents. Specifically, DRL's label will explicitly instruct doctors, pharmacists, other healthcare professionals, and patients to administer DRL's ANDA Product according to methods claimed in one or more claims of the FMF Patents.

49. On information and belief, DRL's label demonstrates DRL's specific intent that, when concomitant administration is necessary or desirable, a doctor, pharmacist, other healthcare professional, or patient administer DRL's ANDA Product according to the instructions on DRL's

labeling regarding dose reduction during concomitant administration and thus directly infringe one or more of claims of the FMF Patents.

50. On information and belief, some FMF patients will undergo concomitant treatment with colchicine for FMF and ketoconazole for a fungal infection.

51. On information and belief, some FMF patients will undergo concomitant treatment with colchicine for FMF and ritonavir for HIV or other viral infections.

52. On information and belief, some FMF patients will undergo concomitant treatment with colchicine for FMF and clarithromycin for bacterial infections, including *H. pylori*.

53. On information and belief, patients concomitantly taking ketoconazole, ritonavir, and/or clarithromycin with colchicine will be prescribed DRL's ANDA Product according to the instructions on DRL's labeling regarding dose reductions in accordance with Takeda's FMF Patents by doctors or other healthcare professionals. Such doctors, healthcare professionals, and patients thus will directly infringe one or more of claims of the FMF Patents.

DRL's INFRINGEMENT OF THE GOUT PATENTS

54. If DRL's ANDA Product is approved by the FDA, DRL will contribute to the infringement of one or more claims of the Gout Patents.

55. On information and belief, DRL has knowledge of Takeda's Gout Patents, which are listed in the Orange Book for Colcrys® and for which, on information and belief, DRL has submitted a section viii carve-out statement to the FDA.

56. On information and belief, DRL's ANDA Product will be administered for the treatment and prophylaxis of acute gout flares.

57. Doctors, pharmacists, other healthcare professionals, and patients will administer DRL's ANDA Product according to the instructions on the Colcrys® labeling regarding the treatment of acute gout flares and will thus infringe one or more claims of the Gout Patents.

58. On information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and ketoconazole for a fungal infection.

59. On information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and ritonavir for HIV or other viral infections.

60. On information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and clarithromycin for bacterial infections, including *H. pylori*.

61. On information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and verapamil for hypertension, angina pectoris, cardia arrhythmia, and/or other disorders.

62. On information and belief, patients concomitantly taking ketoconazole, ritonavir, clarithromycin, and/or verapamil with colchicine will be prescribed DRL's ANDA Product according to the instructions on the Colcrys® labeling regarding dose reductions in accordance with Takeda's Gout Patents by doctors or other healthcare professionals. Such doctors, healthcare professionals and patients thus will directly infringe one or more of claims of the Gout Patents.

63. Upon information and belief, DRL has made, and continues to make, substantial preparations in the United States for the commercial manufacture, use, offer for sale, sale, and/or importation of its ANDA Product prior to the expiration of Takeda's Colcrys® Patents.

64. DRL's actions, including, but not limited to, the development of its ANDA Product and the filing of ANDA No. 209876, indicate a refusal to change the course of its actions despite its knowledge of Takeda's unexpired Colcrys® Patents.

65. Upon information and belief, DRL continues to seek approval of ANDA No. 209876 from the FDA to engage in the commercial use, manufacture, sale, offer for sale, or importation of its ANDA Product prior to the expiration of Takeda's Colcrys® Patents.

66. Upon information and belief, DRL intends to manufacture, offer for sale, and sell its ANDA Product in quantities that far exceed the market for treatment of FMF. Upon information and belief, DRL knows of Takeda's Gout Patents, and knows that its generic version of Colcrys® will be sold to the gout market for the treatment and prevention of gout flares in a manner that infringes Takeda's Gout Patents.

67. DRL's ANDA Product is especially made or adapted for use in connection with the methods of treating and preventing acute gout flares recited by the Gout Patents. DRL's ANDA Product is a 0.6 mg colchicine tablet that is, on information and belief, equivalent to Colcrys®.

68. DRL's ANDA Product is a material part of the claimed inventions. DRL's ANDA Product constitutes a 0.6 mg colchicine dosage form that can be used to practice the claimed inventions.

69. On information and belief, DRL's ANDA Product will be substantially used for the treatment and prevention of gout flares. The primary indication for Colcrys®, and the one

responsible for the vast majority of Colcrys® sales, is gout, which affects far more patients in the United States than does FMF.

70. DRL has sought FDA approval to sell its generic version of Takeda's colchicine product Colcrys® only to treat FMF. On information and belief, DRL has "carved out" the gout indication from its label, thus certifying to the FDA that it will not market its ANDA Product for the treatment of gout.

71. Despite DRL's representations, DRL's ANDA Product will be sold to the gout market and will be used to treat and prevent gout flares, including in patients concomitantly taking ketoconazole, ritonavir, clarithromycin, and/or verapamil. This is because, as discussed above, physicians generally prescribe generic drugs for all of the approved indications associated with the branded drug, whether or not the generic drug is approved for that indication

72. Moreover, many pharmacies will fill Colcrys or colchicine prescriptions to gout patients with DRL's ANDA Product. In some states, such substitution will be mandatory and required by law. In others, individual pharmacists will be incentivized to substitute DRL's ANDA Product for Colcrys because of the lower patient cost and larger pharmacy profit margins associated with generic products.

73. A substantial part of the uses in the gout market will infringe Takeda's patented low-dose method of using colchicine to treat acute gout flares or Takeda's patented methods of using colchicine to prevent or treat gout flares in patients concomitantly taking ketoconazole, ritonavir, clarithromycin, and/or verapamil, because Takeda's patented methods represent the standard of care for gout flare treatment and prevention. *See supra* ¶¶ 22-24.

74. Because DRL has disclaimed any intent to market its ANDA Product to the gout market and has committed to solely marketing its product for the treatment of FMF, the only

purportedly "non-infringing use" for DRL's ANDA Product upon which DRL should be allowed to rely is the use of that product to treat FMF.

75. Taken in their entirety, the uses of DRL's ANDA Product to treat FMF will be insubstantial in comparison to the anticipated overwhelming off-label use of DRL's ANDA Product according to the patented methods of Takeda's Gout Patents. Accordingly, DRL's ANDA Product is not a staple article of commerce capable of substantial non-infringing uses.

EXCEPTIONAL CASE

76. On information and belief, DRL is aware of all of the Colcrys® Patents.

77. DRL had no basis for submitting ANDA No. 209876 or a Paragraph IV Certification. DRL's actions render this an exceptional case under 35 U.S.C. § 285.

COUNT I

(Infringement of the '519 Patent)

78. Paragraphs 1 to 77 are incorporated herein as set forth above.

79. DRL has committed an act of infringement of the '519 Patent that creates a justiciable case or controversy between Takeda and DRL.

80. DRL's submission of its ANDA No. 209876 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of DRL's ANDA Product to treat FMF prior to expiration of the '519 Patent constitutes infringement of claim 1 of the '519 Patent under 35 U.S.C. § 271(e)(2)(A).

81. Unless enjoined by the Court, upon FDA approval of ANDA No. 209876, DRL will induce infringement of the '519 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell DRL's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 209876, DRL will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, DRL's

ANDA Product with knowledge of the ’519 Patent and knowledge that its acts are encouraging infringement.

82. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

83. Takeda does not have an adequate remedy at law.

COUNT II

(Infringement of the ’731 Patent)

84. Paragraphs 1 to 83 are incorporated herein as set forth above.

85. DRL has committed an act of infringement of the ’731 Patent that creates a justiciable case or controversy between Takeda and DRL.

86. DRL’s submission of its ANDA No. 209876 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of DRL’s ANDA Product to treat FMF prior to expiration of the ’731 Patent constitutes infringement of claim 1 of the ’731 Patent under 35 U.S.C. § 271(e)(2)(A).

87. Unless enjoined by the Court, upon FDA approval of ANDA No. 209876, DRL will induce infringement of the ’731 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell DRL’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 209876, DRL will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, DRL’s ANDA Product with knowledge of the ’731 Patent and knowledge that its acts are encouraging infringement.

88. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

89. Takeda does not have an adequate remedy at law.

COUNT III

(Infringement of the ’298 Patent)

90. Paragraphs 1 to 89 are incorporated herein as set forth above.

91. DRL has committed an act of infringement of the ’298 Patent that creates a justiciable case or controversy between Takeda and DRL.

92. DRL’s submission of its ANDA No. 209876 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of DRL’s ANDA Product to treat FMF prior to expiration of the ’298 Patent constitutes infringement of one or more claims of the ’298 Patent, including at least claim 1 of the ’298 Patent, under 35 U.S.C. § 271(e)(2)(A).

93. Unless enjoined by the Court, upon FDA approval of ANDA No. 209876, DRL will induce infringement of the ’298 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell DRL’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 209876, DRL will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, DRL’s ANDA Product with knowledge of the ’298 Patent and knowledge that its acts are encouraging infringement.

94. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

95. Takeda does not have an adequate remedy at law.

COUNT IV

(Infringement of the ’648 Patent)

96. Paragraphs 1 to 95 are incorporated herein as set forth above.

97. DRL has committed an act of infringement of the ’648 Patent that creates a justiciable case or controversy between Takeda and DRL.

98. DRL's submission of its ANDA No. 209876 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of DRL's ANDA Product to treat FMF prior to expiration of the '648 Patent constitutes infringement of one or more claims of the '648 Patent, including at least claim 1 of the '648 Patent, under 35 U.S.C. § 271(e)(2)(A).

99. Unless enjoined by the Court, upon FDA approval of ANDA No. 209876, DRL will induce infringement of the '648 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell DRL's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 209876, DRL will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, DRL's ANDA Product for the treatment of FMF with knowledge of the '648 Patent and knowledge that its acts are encouraging infringement.

100. DRL has knowledge of the '648 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the '648 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the treatment and prevention of gout flares, knowing the same to be especially made for use in infringement of the '648 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

101. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the '648 Patent with respect to the use of DRL's ANDA Product to prevent and treat gout flares. Takeda is entitled to a declaration that DRL's manufacture, use, sale, offer for sale, and/or importation of DRL's ANDA Product will

contribute to the infringement of one or more claims of the ’648 Patent, including at least claim 1 of the ’648 patent, and that the claims of the ’648 Patent are valid.

102. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

103. Takeda does not have an adequate remedy at law.

COUNT V

(Infringement of the ’297 Patent)

104. Paragraphs 1 to 103 are incorporated herein as set forth above.

105. DRL has committed an act of infringement of the ’297 Patent that creates a justiciable case or controversy between Takeda and DRL.

106. DRL’s submission of its ANDA No. 209876 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of DRL’s ANDA Product to treat FMF prior to expiration of the ’297 Patent constitutes infringement of one or more claims of the ’297 Patent, including at least claim 1 of the ’297 Patent, under 35 U.S.C. § 271(e)(2)(A).

107. Unless enjoined by the Court, upon FDA approval of ANDA No. 209876, DRL will induce infringement of the ’297 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell DRL’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 209876, DRL will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, DRL’s ANDA Product for the treatment of FMF with knowledge of the ’297 Patent and knowledge that its acts are encouraging infringement.

108. DRL has knowledge of the ’297 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’297 Patent by others, by offering to sell, selling, or distributing within the

United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the ’297 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

109. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’297 Patent with respect to the use of the DRL ANDA Product to prevent and treat gout flares. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the ’297 Patent, including at least claim 1 of the ’297 patent, and that the claims of the ’297 Patent are valid.

110. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

111. Takeda does not have an adequate remedy at law.

COUNT VI

(Infringement of the ’004 Patent)

112. Paragraphs 1 to 111 are incorporated herein as set forth above.

113. DRL has knowledge of the ’004 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’004 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the treatment and prevention of gout flares, knowing the same to be especially made for use in infringement of the ’004 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

114. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’004 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims, including at least claim 5 of the ’004 Patent, of the ’004 Patent and that the claims of the ’004 Patent are valid.

115. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

116. Takeda does not have an adequate remedy at law.

COUNT VII

(Infringement of the ’758 Patent)

117. Paragraphs 1 to 116 are incorporated herein as set forth above.

118. DRL has knowledge of the ’758 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’758 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the treatment and prevention of gout flares, knowing the same to be especially made for use in infringement of the ’758 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

119. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’758 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the ’758 Patent, including at least claim 10 of the ’758 Patent, and that the claims of the ’758 Patent are valid.

120. Takeda will be irreparably harmed by DRL's infringing activities unless those activities are enjoined by this Court.

121. Takeda does not have an adequate remedy at law.

COUNT VIII

(Infringement of the '681 Patent)

122. Paragraphs 1 to 121 are incorporated herein as set forth above.

123. DRL has knowledge of the '681 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the '681 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the treatment and prevention of gout flares, knowing the same to be especially made for use in infringement of the '681 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

124. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the '681 Patent. Takeda is entitled to a declaration that DRL's manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the '681 Patent, including at least claim 1 of the '681 Patent, and that the claims of the '681 Patent are valid.

125. Takeda will be irreparably harmed by DRL's infringing activities unless those activities are enjoined by this Court.

126. Takeda does not have an adequate remedy at law.

COUNT IX

(Infringement of the '269 Patent)

127. Paragraphs 1 to 126 are incorporated herein as set forth above.

128. DRL has knowledge of the ’269 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’269 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the treatment and prevention of gout flares, knowing the same to be especially made for use in infringement of the ’269 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

129. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’269 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of claim 1 of the ’269 Patent, and that the claims of the ’269 Patent are valid.

130. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

131. Takeda does not have an adequate remedy at law.

COUNT X

(Infringement of the ’647 Patent)

132. Paragraphs 1 to 131 are incorporated herein as set forth above.

133. DRL has knowledge of the ’647 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’647 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the

’647 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

134. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’647 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of claim 1 of the ’647 Patent and that the claims of the ’647 Patent are valid.

135. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

136. Takeda does not have an adequate remedy at law.

COUNT XI

(Infringement of the ’938 Patent)

137. Paragraphs 1 to 136 are incorporated herein as set forth above.

138. DRL has knowledge of the’938 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’938 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the ’938 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

139. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’938 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will

contribute to the infringement of claim 1 of the ’938 Patent and that the claims of the ’938 Patent are valid.

140. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

141. Takeda does not have an adequate remedy at law.

COUNT XII

(Infringement of the ’296 Patent)

142. Paragraphs 1 to 141 are incorporated herein as set forth above.

143. DRL has knowledge of the ’296 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’296 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the ’296 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

144. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’296 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the ’296 Patent, including at least claim 1 of the ’296 patent, and that the claims of the ’296 Patent are valid.

145. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

146. Takeda does not have an adequate remedy at law.

COUNT XIII

(Infringement of the ’655 Patent)

147. Paragraphs 1 to 146 are incorporated herein as set forth above.

148. DRL has knowledge of the ’655 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’655 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the ’655 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

149. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’655 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the ’655 Patent, including at least claim 1 of the ’655 Patent, and that the claims of the ’655 Patent are valid.

150. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

151. Takeda does not have an adequate remedy at law.

COUNT XIV

(Infringement of the ’395 Patent)

152. Paragraphs 1 to 151 are incorporated herein as set forth above.

153. DRL has knowledge of the ’395 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’395 Patent by others, by offering to sell, selling, or distributing within the

United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the ’395 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

154. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’395 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the ’395 Patent, including at least claim 1 of the ’395 Patent, and that the claims of the ’395 Patent are valid.

155. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

156. Takeda does not have an adequate remedy at law.

COUNT XV

(Infringement of the ’396 Patent)

157. Paragraphs 1 to 156 are incorporated herein as set forth above.

158. DRL has knowledge of the ’396 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’396 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the ’396 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

159. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’396 Patent. Takeda is entitled to a declaration

that DRL's manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the '396 Patent, including at least claim 1 of the '396 Patent, and that the claims of the '396 Patent are valid.

160. Takeda will be irreparably harmed by DRL's infringing activities unless those activities are enjoined by this Court.

161. Takeda does not have an adequate remedy at law.

COUNT XVI

(Infringement of the '721 Patent)

162. Paragraphs 1 to 161 are incorporated herein as set forth above.

163. DRL has knowledge of the '721 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the '721 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the '721 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

164. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the '721 Patent. Takeda is entitled to a declaration that DRL's manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the '721 Patent, including at least claim 1 of the '721 Patent, and that the claims of the '721 Patent are valid.

165. Takeda will be irreparably harmed by DRL's infringing activities unless those activities are enjoined by this Court.

COUNT XVII

(Infringement of the ’722 Patent)

166. Paragraphs 1 to 165 are incorporated herein as set forth above.

167. DRL has knowledge of the ’722 Patent. Unless enjoined by the court, upon approval of ANDA No. 209876, DRL, in violation of 35 U.S.C. § 271(c), will contribute to infringement of the ’722 Patent by others, by offering to sell, selling, or distributing within the United States or importing into the United States the DRL ANDA Product for the prevention and treatment of gout flares, knowing the same to be especially made for use in infringement of the ’722 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

168. There is an actual and justiciable controversy between Takeda and DRL concerning the infringement and validity of the ’722 Patent. Takeda is entitled to a declaration that DRL’s manufacture, use, sale, offer for sale, and/or importation of its ANDA Product will contribute to the infringement of one or more claims of the ’722 Patent, including at least claim 1 of the ’722 Patent, and that the claims of the ’722 Patent are valid.

169. Takeda will be irreparably harmed by DRL’s infringing activities unless those activities are enjoined by this Court.

170. Takeda does not have an adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Takeda requests entry of judgment in its favor and against DRL as follows:

A. For a judgment and decree that DRL has infringed one or more claims of the FMF Patents (the ’519, ’731, ’298, ’648, and ’297 Patents) under 35 U.S.C. § 271(e)(2)(A) by submitting its ANDA No. 209876 with a Paragraph IV Certification seeking approval to

engage in the commercial use, manufacture, sale, offer for sale, or importation of DRL's ANDA Product to treat FMF prior to the expiration of the Patents;

B. For a declaration that the commercial use, sale, offer for sale, manufacture, and/or importation by DRL of its ANDA Product would infringe one of more claims of the FMF Patents (the '519, '731, '298, '648, and '297 Patents) under 35 U.S.C. § 271(b);

C. For a declaration that the commercial use, sale, offer for sale, manufacture, and/or importation by DRL of its ANDA Product would infringe one of more of the claims of the Gout Patents (the '004, '758, '681, '269, '647, '648, '938, '296, '297, '655, '395, '396, '721, and '722 Patents) under 35 U.S.C. § 271(c);

D. For an order preliminarily and permanently enjoining DRL and its affiliates, subsidiaries, directors, employees, agents, representatives, licensees, successors, assigns, and all other persons acting or attempting to act in active concert or participation with it or acting on its behalf, from infringing the Colcrys® Patents;

E. For an order that, if DRL engages in the commercial manufacture, use, importation into the United States, sale, or offer for sale of its ANDA Product before the expiration of the Patents, a judgment be awarded to Takeda for damages resulting from such infringement, together with interest, in an amount to be determined at trial;

F. For an order pursuant to 35 U.S.C. 271(e)(4)(A) that the effective date for approval of ANDA No. 209876, under § 505(j) of the FFDCA (21 U.S.C. § 355(j)), be no earlier than the expiration date of the last of the Colcrys® Patents, including any extensions or adjustments;

G. For an order declaring this an exceptional case under 35 U.S.C. § 285, and awarding to Takeda its reasonable attorneys' fees, costs, and expenses; and

H. For such other and further relief as this Court deems just and proper.

Respectfully submitted,

Date: January 17, 2018

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