BEFORE THE CONTROLLER OF PATENTS

THE PATENT OFFICE BRANCH, DELHI

OPPOSITION BY WAY OF PRE-GRANT REPRESENTATION

In the matter of:

Patent Application No. 4759/DELNP/2012
dated: 29.05.2012

in the name of

AbbVie Inc.
A US Company of
1 North Waukegan Road
North Chicago
IL 60064, USA

and in the matter of

Opposition by way of pre-grant representation
u/Section 25(1) of The Patents Act, 1970
r/w Rule 55 of The Patents Rules 2003
as amended from time to time

filed for and on behalf of:

MSN Laboratories Pvt. Ltd.
An Indian Company,
of MSN House, C24,
Sanath Nagar Industrial Estate, Sanath Nagar
Hyderabad 500 038, Telangana State.

MSN Laboratories Pvt. Ltd. …Opponent

-versus-

AbbVie Inc. …Applicant

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1. We, MSN Laboratories Pvt. Ltd., [hereinafter "***MSN***"] submit our pre-grant representation against grant of patent on IN 4759/DELNP/2012 [hereinafter "***IN'4759***"] titled "*Novel Tricyclic Compounds"* naming AbbVie Inc. [hereinafter "***AbbVie***"] as Assignee/Applicant.

2. MSN is compelled to initiate these proceedings due to the extraordinarily egregious conduct of AbbVie, including communications

forming groundless threats of alleged patent rights which simply do not exist, and also, naming of MSN in communications to the Indian Patent Office [hereinafter "***IPO***"] with unwarranted error-filled assertions, but without providing either advance notice to or copying MSN.

I. Preliminary Submissions:

3. MSN, after a review of available material on the IPO website, notes that multiple pre-grants are pending against IN'4759. MSN, for purposes of brevity of pleadings, also relies on the documents and findings in the First Examination Report and other Examination Reports issued by the IPO, as well as the documents and submissions of other opponents, apart from providing its own submissions as contained hereinafter. For ease of reference, the bibliography of IN'4759 is given below:

IN 4759/DELNP/2012	
Applicant	AbbVie Inc.
Title at filing	*Novel Tricyclic Compounds*
Inventors	Neil Wishart Maria A. Argiriadi David J. Calderwood Anna M. Ericsson Bryan A. Fiamengo Kristine E. Frank Michael Friedman Dawn M. George Eric R. Goedken Nathan S. Josephson Biqin C. Lin Michael J. Morytko Kent. D. Stewart Jeffrey W. Voss Grier A. LaCe Lu Wang Kevin R. Woller
Priority claimed:	01.12.2009 (US 61/265,563) & 14.07.2010 (US 61/364,116)
PCT Details	PCT/US2010/058572 filed on 01.12.2010 published as WO 2011/068881 on 09.06.2011
Filing Date	01.12.2010 (International Filing Date)
Claims	1 currently pending claim

4. This opposition is based, inter alia, on the following grounds from Section 25(1) of The Patents Act, 1970:

a) **Section 25(1)(i)**: that in the case of a convention application, the application was not made within twelve months from the date of the first application for protection for the invention made in a convention country by the applicant or a person from whom he derives title –wrong priority claim;

b) **Section 25(1)(b)**: that the invention of the sole claim of IN'4759 has been published before the priority date thereof in India or elsewhere in any other document –Anticipation by prior publication

c) **Section 25(1)(e)**: that the invention of the sole claim of IN'4759 clearly does not involve any inventive step having regard to the matter published as mentioned in clause (b) –Lack of inventive step

d) **Section 25(1)(e)**: that the invention of the sole claim of IN'4759 is obvious having regard to the matter published as mentioned in clause (b) – What is claimed is obvious to a person of skill in the art

e) **Section 25(1)(f)**: that subject matter of the sole claim of IN'4759 is not an invention within the meaning of this Act, or is not patentable under this Act; i.e., - Not patentable under the Act, including u/Sec.3(d)

f) **Section 25(1)(f)**: that subject matter of the sole claim of IN'4759 is not an invention within the meaning of this Act, or is not patentable under this Act – what is claimed does not fall within the definition of "invention" as defined in Section 2(1)(j)

g) **Section 25(1)(g)**: that the complete specification of IN'4759 does not sufficiently and clearly define the invention or the method by which it is to be performed; i.e., - lack of enabling disclosure or support for what is claimed including its purported technical advantages over prior art;

h) **Section 25(1)(h)**: deliberate non-compliance with section 8 requirements – both Section 8(1) and Section 8(2).

Each ground is taken separately and without prejudice to any other. Reliance on any one ground and submissions made in connection therewith are not to be deemed an abandonment of submissions made under any other ground. In this context, it is settled law that a proceeding under Section 25(1) is in aid of examination proceedings such that patents are granted only for what are truly meritorious inventions and not for attempted evergreening. MSN reserves its right to file further submissions /rely on documents as may be necessary if AbbVie attempts any

amendments, including attempts to incorporate fresh claim(s) – whether with prior notice to MSN or in a surreptitious manner behind MSN's back. MSN prays that it be informed of any amendments to either the complete specification or the claims of IN'4759 so that it can consider its rights in law and, if required, present appropriate submissions.

5. Given below in tabular form for ease of reference is a list of documents relied on in this Opposition, along with short form nomenclature/indicia used herein.

Document with short note where applicable	**Short Form/Indicia**
IN 4759/DELNP/2012 with claim currently pending and with as-filed claims	Annexure 1: IN'4759
WO 2011/068881 – Front Page as published [PCT Publication corresponding to IN'4759]	Annexure 2: WO'881
US Prov. 61/265,563 dated 01.12.2009 [priority document 1 for IN'4759]	Annexure 3: US'563/PD_1
US Prov. 61/364,116 dated 14.07.2010 [priority document 2 for IN'4759]	Annexure 4: US'116/PD_2
Form 1 on IN'4759	Annexure 5
Forms 3 on IN'4759	Annexure 6 Colly.
EPO Opposition Board Decision on EP 10835061.2 Rejecting claim to priority [corr. to IN'4759]	Annexure 7
Decision of PRID on CN104592231A refusing priority	Annexure 8
Decision of PRID on CN102711476B holding invalid	Annexure 9
Decision of PRID on CN109053742B holding invalid	Annexure 10
IPD Analytics Report on CN equivalents of IN'4759	Annexure 11
WO 2009/152133 [belongs to AbbVie and claims Upadacitinib]	D1: WO'133
US Pat. Publ. 2009/0312338 [US Publ. corr. to WO'133, granted as US 8962629]	D2: US'338
US Prov. 61/131,599 dated 10.06.2008 [priority document A for US'338/WO'133]	D3: US'599/PD_A
US Prov. 61/131,602 dated 10.06.2008 [priority document B for US'338/WO'133]	D4: US'602/PD_B
US Prov. 61/190,159 dated 26.08.2008 [priority document C for US'338/WO'133]	D5: US'159/PD_C

US Prov. 61/201,064 dated 05.12.2008 [priority document D for US'338/WO'133]	D6: US'064/PD_D
Orange Book Listing for Upadacitinib	D7: OB
Patent Term Extension Request filed by AbbVie on US Patent 8962629 [corr. WO'133/US'338]	D8: PTE
Australian Patent Certificate for AU2009257602	D9
Extract from Register of Patents for AU 2009257602	D10
Claims granted on AU2009257602	D11
AbbVie's request for Patent Term Extension in AU for AU2009257602 dated 27.02.2020 with AbbVie's Claim Construction	D12
AU Patent Office Letter of 06.07.2020 granting PTE on AU2009257602 for Upadacitinib	D13
Form 1 of IN195/DELNP/2011 granted as IN292307 [corr. to WO'133/US'338]	D14
Form 3 of IN 195/DELNP/2011 granted as IN292307 [corr. to WO'133/US'338]	D15 Colly.
WO 2009/106442 published on 03.09.2009	D16: WO'442
Kremer et al, "*Safety and Efficacy of a JAK Inhibitor in Patients with Active Rheumatoid Arthritis*", Vol. 60, No. 7, July 2009, pp. 1895-1905. DOI 10.1002/art.24567	D17: Kremer
Williams et al., "*Dissecting Specificity in the Janus Kinases: The Structures of JAK-Specific Inhibitors Complexed to the JAK1 and JAK2 Protein Tyrosine Kinase Domains";* J.Mol.Biol., (Jan 2009) 387, 219-232	D18: Williams et al

6. MSN reserves its right to file such further documents and make assertions/averments/submissions as may be necessary to address any answer that AbbVie may provide to this opposition statement.

7. The file history of IN'4759 reveals that practically every opponent has raised serious questions regarding the validity of priority claims on IN'4759. The essence of the challenge is that pending Claim 1 [for a compound named Upadacitinib and its pharmaceutically acceptable salts] has no basis in the text/claims of US'563/PD_1. A part of this challenge has been that Upadacitinib finds its first mention only in the complete

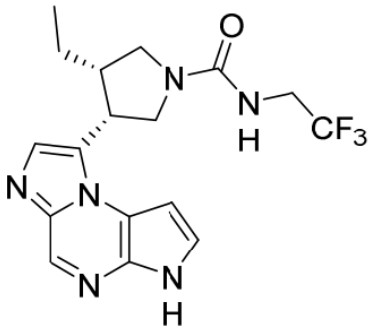
specification of WO'881 i.e., PCT precursor to IN'4759. Thus, IN'4759 to the extent that claim is limited to Upadacitinib is entitled to a priority of 01.12.2010 i.e., international filing date of WO'881, and not the claimed priorities of 01.12.2009 [US'563/PD_1] or 14.07.2010 [US'116/PD_2].

8. Strong support for this challenge to priority claim resides in the fact that AbbVie voluntarily and consciously chose not to contest this challenge in Europe in an opposition to the corresponding European Patent Application EP10835061.2 [**Annexure 7, paragraph II.3.**]. Thus, AbbVie by its conduct in Europe in not choosing to comment accepted that it is not entitled to the originally claimed priority dates of 01.12.2009 or 14.07.2010.

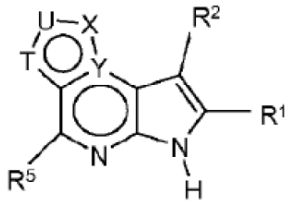
9. It would appear that similar rejection of priority claim on the corresponding Chinese Application has also been accepted by AbbVie without demur. Copies of decisions in relation to the corresponding Chinese applications are attached herewith as **Annexures 8 to 10**, along with a short English language report from a reputed IP News Agency, viz., IPD Analytics [**Annexure 11**]. Opponent undertakes to file English language translations of the decisions shortly.

10. In direct contrast, in the various proceedings on IN'4759, AbbVie adopts a contrary position – that it is, in fact, entitled to the claimed priorities. AbbVie sets out in its various responses to the IPO on other pre-grants what it asserts as the foundation of its priority claim. A summary of AbbVie's position in India on IN'4759 is given below:

Upadacitinib Structure as per Claim 1 of IN'4759:

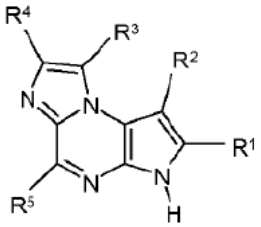


Derivation of Upadacitinib from US'563/PD_1 [allegedly fairly based/enabled]



Formula I

a. In the structure of Formula I, when T is N, U is CR^4, X is CR^3 and Y is N, then the compound has the following structure:



Formula Ic – allegedly present in Claim 17 of US'563/PD_1. Formula Ic leads to/gives Upadacitinib when

b. R^1, R^2 and R^5 are each independently hydrogen [page 307 of US'563/PD_1]

c. R^4 is hydrogen [page 309 of US'563/PD_1]

Derivation Explanation I : where G is an amide:

d. R^3 is -A-D-E-G, where

: A is a bond [claim 2]

: D is an optionally substituted (C_2-C_{10})heterocyclolene [claim 3], optionally substituted pyrrolidine [Claim 4]

: E is a bond [Claim 5]

: G is [-C(O)N(R^a)(R^b)] [Claims 6 and 7]

: R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl where the "optional substituents" are defined on page 44 of US'563/PD_1 as including halogenated (C_1-C_8) alkyl group, i.e., trifluoroethyl.

Derivation Explanation II: where E is an amide:

d. R^3 is -A-D-E-G, where

: A is a bond [claim 2]

: D is an optionally substituted (C_2-C_{10})heterocyclolene [claim 3], optionally substituted pyrrolidine [Claim 4]

: G is CF_3

: E is [-C(O)N(R^a)(R^b)]

: R^a is H

: R^e for each occurrence is independently a bond or an optionally substituted (C_1-C_{10}) alkylene.

11. AbbVie asserts that these alternative explanations provide "fair basis/enablement" for Upadacitinib. This explanation for priority claim support is provided by AbbVie by cherry-picking from disclosure including substitutions for the Markush structure provided in US'563/PD_1. Critically, what is admitted is that there is no express disclosure of Upadacitinib in the US'563/PD_1. Without admitting either accuracy of AbbVie's hindsight cherry-picked and jerry-rigged justification for priority, MSN presents its submissions on its grounds of opposition.

II. Section 25(1)(i): IN'4759 should be refused since it was not filed within 12 months of the earliest application from which priority could have been claimed:

12. The relevant provisions are present in Chapter XXII of The Act, in particular Sections 135, 137, and 139 [reproduced below]:

> S.135(1) Without prejudice to the provisions contained in section 6, where a person has made an application for a patent in respect of an invention in a convention country (hereinafter referred to as the "basic application"), and that person or the legal representative or assignee of that person makes an application under this Act for a patent within twelve months after the date on which the basic application was made, the priority date of a claim of the complete specification, being a claim based on matter disclosed in the basic application, is the date of making of the basic application.
> *Explanation* - Where applications have been made for similar protection in respect of an invention in two or more convention countries, the period of twelve months referred to in this sub-section shall be reckoned from the date on which the earlier or earliest of the said applications was made.
>
> S.136(1) Special provisions relating to convention applications.—
> (1) Every convention application shall—
> (a) be accompanied by a complete specification; and
> (b) specify the date on which and the convention country in which the application for protection, or as the case may be, the first of such applications was made; and
> (c) state that no application for protection in respect of the invention had been made in a convention country before that date by the applicant or by any person from whom he derives title.
>
> S. 137(1) Where two or more applications for patents in respect of inventions have been made in one or more convention countries and those inventions are so related as to constitute one invention, one

application may be made by any or all of the persons referred to in sub-section *(1)* of section 135 within twelve months from the date on which the earlier or earliest of those applications was made, in respect of the inventions disclosed in the specifications which accompanied the basic applications.
(2) The priority date of a claim of the complete specification, being a claim based on matters disclosed in one or more of the basic applications, is the date on which that matter was first so disclosed.
(3) For the purposes of this Act, a matter shall be deemed to have been disclosed in a basic application for protection in a convention country if it was claimed or disclosed (otherwise than by way of disclaimer or acknowledgment of prior art) in that application, or any documents submitted by the applicant for protection in support of and at the same time as that application, but no account shall be taken of any disclosure effected by any such document unless a copy of the document is filed at the patent office with the convention application or within such period as may be prescribed after the filing of that application.
S.138(4). An international application filed under the Patent Cooperation Treaty designating India shall have effect of filing an application for patent under section 7, section 54 and section 135, as the case may be, and the title, description, claim and abstract and drawings, if any, filed in the international application shall be taken as complete specification for the purposes of this Act.
S.139. Other provisions of Act to apply to convention applications .—Save as otherwise provided in this Chapter, all the provisions of this Act shall apply in relation to a convention application and a patent granted in pursuance thereof as they apply in relation to an ordinary application and a patent granted in pursuance thereof.

13. MSN relies on the following documents, each of which individually provide and form the basis of a priority claim in respect of Upadacitinib. Pertinently, the standard adopted for determining this priority claim basis is exactly as adopted by AbbVie qua US'563/PD_1. Equally, pertinently, the documents relied on are all also of AbbVie or its predecessor and pertinently have the same set of inventors.

a. US'338/D2 dated 09.06.2009
b. US'599/D3 dated 10.06.2008
c. US'602/D4 dated 10.06.2008
d. US'159/D5 dated 26.08.2008
e. US'064/D6 dated 05.12.2008

14. Documents (b) to (e) in paragraph 13 above are priority documents for Document (a), viz., US'338, which corresponds to WO'133, i.e., D1, which in turn resulted in an earlier patent of AbbVie, viz., IN 292307.

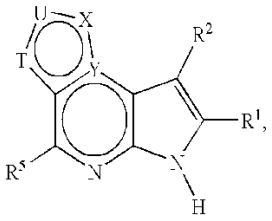
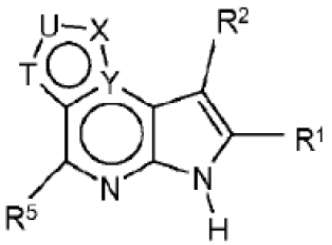
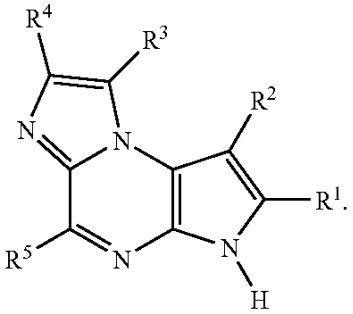
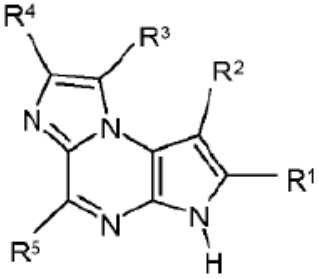
15. For ease of reference (and convenience), how priority for Upadacitinib is there in each such document is given below as a tabular comparison as was done by AbbVie qua US'563/PD_1.

A. **US'338/D2::**

16. US'338 is dated 09.06.2009, i.e., ***six (6) months before*** the earliest priority date of 01.12.2009 claimed on IN'4759. For ease of reference, a bibliographic comparison of US'338/D2 and IN'4759 is given below:

US 8962629	**Detail**	**IN'4759**
AbbVie Inc.	Assignee	AbbVie Inc.
Novel Tricyclic Compounds	Title at filing	*Novel Tricyclic Compounds*
Neil Wishart Maria A. Argiriadi David J. Calderwood Anna M. Ericsson Bryan A. Fiamengo Kristine E. Frank Michael Friedman Dawn M. George Eric R. Goedken Nathan S. Josephson Biqin C. Lin Michael J. Morytko Kent. D. Stewart Jeffrey W. Voss Grier A. LaCe Lu Wang Kevin R. Woller	Inventors	Neil Wishart Maria A. Argiriadi David J. Calderwood Anna M. Ericsson Bryan A. Fiamengo Kristine E. Frank Michael Friedman Dawn M. George Eric R. Goedken Nathan S. Josephson Biqin C. Lin Michael J. Morytko Kent. D. Stewart Jeffrey W. Voss Grier A. LaCe Lu Wang Kevin R. Woller
10.06.2008 (US 61/131,599) 10.06.2008 (US 61/131,602) 26.08.2008 (US 61/190,159 & 05.12.2008 (US 61/201,064)	Priority claimed:	01.12.2009 (US 61/265,563) & 14.07.2010 (US 61/364,116)
Corr. to PCT/US2009/046714 filed on 09.06.2009 published as WO 2009/0152133 on 17.12.2009	PCT Details	PCT/US2010/058572 filed on 01.12.2010 published as WO 2011/068881 on 09.06.2011
09.06.2009	Filing Date	01.12.2010 (International Filing Date)
Claims Upadacitinib as per AbbVie in submissions to USPTO via Patent Term Extension Request [Pl. See D8/PTE]	Claims	1 currently pending claim

17. The Table given below captures exactly how [adopting the same protocol as AbbVie] Upadacitinib is fairly based on the description of US'338/D2 which was filed on ***09.06.2009 – almost 18 months before the international filing date of IN'4759 of 01.12.2010.***

US'338 dated 09.06.2009	**US'563 dated 01.12.2009**
A. Structure: In a first embodiment the invention provides a compound of Formula (I) Formula (I)  pharmaceutically acceptable salts, …wherein **[Page 1, Para 0004]**	***A. Structure***:  Formula (I)
B. Substitutions: when T is N, U is CR^4, X is CR^3 and Y is N, **[Page 1, Para 0007]** then the compound has the following structure:  Formula Ic **[Page 12, Para 0174]** and R^1, R^2 and R^5 are each independently hydrogen **[Page 1, Para 0014]** and R^4 is hydrogen **[Page 2, Para 0025]**.	***B. Substitutions***: when T is N, U is CR^4, X is CR^3 and Y is N, then the compound has the following structure:  Formula (Ic) – allegedly present in Claim 17 of US'563/PD_1 and R^1, R^2 and R^5 are each independently hydrogen [page 307 of US'563/PD_1] and R^4 is hydrogen [page 309 of US'563/PD_1]
C. Alternative I when G is an amide: R^3 is -A-D-E-G, **[Page 1, Para 0017]** where A is a bond **[Page 1, Para 0018]**	***C. Alternative I when G is an amide***: R^3 is -A-D-E-G, where A is a bond [claim 2]

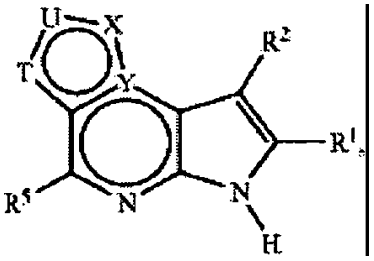
D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 1, Para 0019]**, optionally substituted pyrrolidine **[Page 11, Para 0157]** E is a bond **[Page 1, Para 0020]** G is [-C(O)N(R^a)(R^b)] **[Page 2, Para 0023]** R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl **[Page 2, Para 0033]** where the "*optional substituents*" include halogenated (C_1-C_8) alkyl group, i.e., CF_3 **[Page 33, Para 0369**.	D is an optionally substituted (C_2-C_{10}) heterocyclolene [claim 3], and optionally substituted pyrrolidine [Claim 4] E is a bond [Claim 5] G is [-C(O)N(R^a)(R^b)] [Claims 6 and 7] R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl where the "optional substituents" are defined on page 44 of US'563/PD_1 as including halogenated (C_1-C_8) alkyl group, i.e., CF_3.
D. Alternative II when E is amide: R^3 is -A-D-E-G, **[Page 1, Para 0017]** where A is a bond **[Page 1, Para 0018]** D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 1, Para 0019]**, optionally substituted pyrrolidine **[Page 11, Para 0157]** G is CF_3 **[Page 2, Para 0023]** E is [-C(O)N(R^a)(R^b)] **[Page 1, Para 0020]** R^a is H **[Page 2, Para 0033]** R^e for each occurrence is independently a bond or an optionally substituted (C_1-C_{10}) alkylene. **[Page 2, Para 0034]**.	***D. Alternative II when E is amide***: R^3 is -A-D-E-G, where A is a bond [claim 2] D is an optionally substituted (C_2-C_{10}) heterocyclolene [claim 3], optionally substituted pyrrolidine [Claim 4] G is CF_3 E is [-C(O)N(R^a)(R^b)] R^a is H R^e for each occurrence is independently a bond or an optionally substituted (C_1-C_{10}) alkylene.

18. MSN respectfully submits that the extracts from US'338 referred to above are exemplars – the same text [which according to AbbVie provides priority claim support when present in US'563] is present in multiple locations within US'338 – reliance will be placed on all such references at the hearing. In fact, what is peculiar is that large swathes of description of IN'4739 are actually lifted lock, stock and barrel from US'338 as well as its priority forming applications, but there is no reference at all to this art in IN'4759.

19. Support for the fact that priority could have been claimed on IN'4759 [which claims Upadacitinib] from US'338 resides in submissions of AbbVie to the USPTO. AbbVie filed a patent term extension request to the USPTO that is filed in this opposition as Document D8/PTE. It is AbbVie's categorical assertion to the USPTO that US Patent 8962629 granted on US'338 claims Upadacitinib. Relevant extracts of AbbVie's communication to the USPTO dated 08.10.2019 are given below for ease of reference:

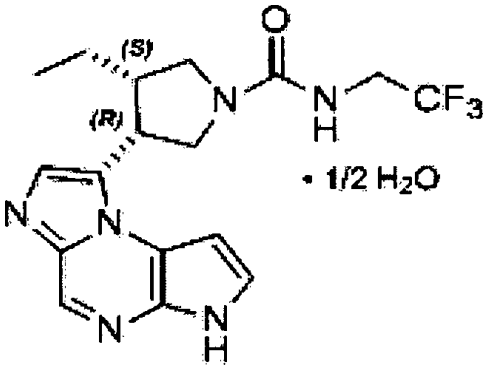
> [***internal page 1***]
> "Pursuant to 35 U.S.C. § 156 and 37 C.F.R. §§ 1.710 to 1.791, AbbVie Inc. ("Applicant" or "AbbVie") herewith applies for an extension of the term of U.S. Patent No. 8,962,629 **(Exhibit 1,** "the '629 patent"). As permitted by 37 C.F.R. § 1.785 and MPEP § 2761, Applicant is concurrently filing a request for patent term extension of U.S. Patent No. RE47,221, based upon the same regulatory review period."
>
> [***internal page 2***]
> "The approved product that is relevant to this Application is RINVOQ™ (upadacitinib) extended-release tablets, for oral use, referred to herein as "RINVOQ" or "Approved Product." The Marketing Applicant for RINVOQ is AbbVie Inc., the same entity as Applicant. Accordingly, Applicant relies on its own activities, and that of its predecessors, and affiliates for purposes of this Application For Extension of Patent Term Under 35 U.S.C. § 156."
>
> [***internal page 7***]
> "(9) A STATEMENT THAT THE PATENT CLAIMS THE APPROVED PRODUCT, OR A METHOD OF USING OR MANUFACTURING THE APPROVED PRODUCT, AND A SHOWING WHICH LISTS EACH APPLICABLE PATENT CLAIM AND DEMONSTRATES THE MANNER IN WHICH AT LEAST ONE SUCH PATENT CLAIM READS ON THE APPROVED PRODUCT OR A METHOD OF USING OR MANUFACTURING THE APPROVED PRODUCT:
>
> [***internal page 8-12***]
> "The '629 patent claims the Approved Product. At least claims 1, 4, 11-16, and 28[1] read on the Approved Product. Moreover, at least claims 51 to 53[2] read on methods of using the Approved Product.
>
> Pursuant to 37 C.F.R. § l.740(a)(9), a showing which demonstrates the manner in which at least one patent claim reads on the Approved Product is set forth below.

Claim 1 reads on the Approved Product. That is, claim 1, which is set forth in full in **Exhibit 1,** is directed to compounds of Formula (I):



Formula (I)

As noted in section 1 of this Application, upadacitinib, the active ingredient in RINVOQ has the following structural formula:



See Approved Labeling (Exhibit 3), Section 11 Description.

The structure described as Formula (I) in claim 1 reads on upadacitinib, for example, when:

a) T is N, U is CR4, X is CR[3], and Y is **N;**
b) R[1] and **R[2]** are each hydrogen;
c) R[5] is hydrogen;
d) R[4] is a hydrogen; and
e) R[3] is -A-D-E-G, [3] wherein:

- A is a bond;
- Dis an optionally substituted (C2-C10)heterocyclylene;
- **E is —R[e]C(O)N(R[a])R[e]—;[4]**
- G is an optionally substituted -(C1-C6)alky1;[5]

a) *R[a]* is a hydrogen; and
b) *Re* is a bond.

When defining the possible substituents for claim 1 as discussed above such that the claim reads on the Approved Product, claims 4, and 13-16 also then read on the Approved Product as discussed further below.

Claim 4, which is dependent on claim 1, reads on the Approved Product when, as discussed above for claim 1, T is N, U is CR4, X is CR3, and Y is N, which forms a compound of Formula (le).

Claim 13, which is dependent on claim 1, reads on the Approved Product when R^3 in claims 1 and 13 is -A-D-E-G and A is a bond.
Claim 14, which is dependent on claim 13, reads on the Approved Product when, in addition to the selections noted above for claims 1 and 13, D in claim 1 is an optionally substituted (C2-C10)heterocyclylene, and Din claim 14 is an optionally substituted pyrrolidinyl.
Claim 15, which is dependent on claim 14, reads on the Approved Product when, in addition to the selections noted above for claims 1, 13, and 14, E in claims 1 and 15 is $—R^eC(O)N(R^a)R^e—$.
Also, claim 16, which is dependent on claim 15, reads on the Approved Product when, in addition to the selections noted above for claims 1, and 13-15, Gin claims 1 and 16 is optionally substituted (C1-C6)alkyl.
In addition, claims 51 and. 52 read on methods of using the Approved Product and recite as follows:

a) A method of treating or ameliorating a disease or disorder in an individual in need thereof, comprising administering to the individual a compound of claim 1, wherein the disease or disorder is rheumatoid arthritis (RA), psoriasis, juvenile rheumatoid arthritis (JRA), Crohn's disease, psoriatic arthritis, ankylosing spondylitis, or ulcerative colitis.
b) The method of claim 51, wherein disease or disorder is rheumatoid arthritis (RA).

[relevant footnotes reproduced below:]

[1] Claim 11, which is dependent on claim 1, reads on the Approved Product when R^3 in claims 1 and 11 is an optionally substituted (C2-C10)heterocyclyl. The term "heterocyclyl" is defined as "non- aromatic, ring systems, including, but not limited to, monocyclic, bicyclic, tricyclic and spirocyclic rings, which can be completely saturated or which can contain one or more units of unsaturation, for the avoidance of doubt, the degree of unsaturation does not result in an aromatic ring system) and have 5 to 12 atoms including at least one heteroatom, such as nitrogen, oxygen, or sulfur." ('629 patent, 56:51-58).

Claim 12, which is dependent on claim 11, reads on the Approved Product when **R^3** in claims **1** and 11 is an optionally substituted (C2-C 10) heterocyclyl, and R^3 in claim 12 is an optionally substituted pyrrolidinyl.

Claim 28, which is dependent on claim 11, also reads on the Approved Product when, in addition to the selections noted above for claims 1 and 11, R2 and R^5 are each hydrogen.

[2] Claim 53 recites a method of using the Approved Product not currently approved by FDA. It is Applicant's understanding that such a claim nonetheless should be included in the listing of claims pursuant to 37 C.F.R. § 1.740."

[3] Alternatively, as discussed earlier, *supra* note 1, Claims 1, 11, 12, and 28 read on the Approved
Product if R^3 in claim 1 is an optionally substituted (C2-C 10)heterocyclyl (instead of A-D-E-G). The selections for T, U, **X, Y, R**1, R2, **R^4** and R^5 would be the same as defined above.

[4] Alternatively, Claim 1 reads on the Approved Product if Eis a bond, G is -C(O)N(Ra)(Rb), *Ra* is a hydrogen, and *Rb* is an optionally substituted (C1-C10) alkyl. The selections for T, U, **X, Y,** R1, **R^2,** R4, R^5, and R3, A and D would be the same as defined above.

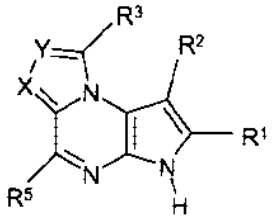
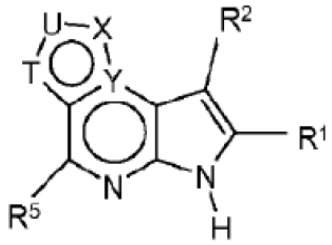
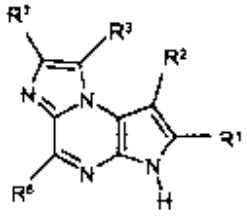
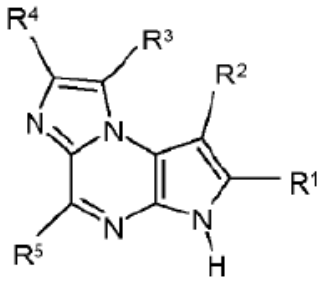
5 Alternatively, Claim 1 reads on the Approved Product if G is CF3, one *Re* is a bond, the other *Re* is an optionally substituted alkylene, Ra is hydrogen, and selections for T, U, **X, Y,** R1, R2, R4, R^5, R3, A, D, and E are as defined above."

20. In the light of an admitted position of AbbVie, and before an authority competent to consider and adjudicate on such position/prayer, viz., the USPTO, there can be no doubt that US'338 provides fair basis for Upadacitinib. Thus, priority could have been claimed on IN'4759 from US'338/D2 but was not. IN'4759 was filed after 12 months from such application. Thus, IN'4759 is liable to be refused on this ground alone.

B. US'064/D6:

21. US'064 is the fourth priority document for US'338/D2. US'064 has an acknowledged ***filing date of 05.12.2008 – i.e., almost 24 months before the filing date of IN'4759 of 01.12.2010***. The tabular comparison below shows how each element of Upadacitinib as claimed in the sole subsisting claim of IN'4759 finds disclosure and on a fair basis in US'064.

US'064 dated 05.12.2008	**US'563 dated 01.12.2009**
E. Structure: In a first embodiment the invention provides a compound of Formula (I)	***E. Structure***:

 Formula (I) pharmaceutically acceptable salts, …wherein **[Page 1, last paragraph]** *Note: the nomenclature of substitutions is slightly different in US'064 as shown below:* *T in IN'4759 = X in US'064* *Y in IN'4759 = N in US'064* *U in IN'4759 = Y in US'064* *X in IN'4759 = CR3 in US'064*	 Formula (I)
F. Substitutions: when X i.e., T of IN'4759 is N, Y i.e., U of IN'4759 is CR^7, X is already CR^3 and Y is already N, **[Page 1-2, bridging paragraphs]** Then the compound has the following structure:  Formula (Ic) Formula Ic **[Page 6, lines 10-11]** and R^1, R^2 & R^5 are each independently hydrogen **[Page 2, line 1]** and R^7 is hydrogen **[Page 4, line 14]**.	***F. Substitutions***: when T is N, U is CR^4, X is CR^3 and Y is N, then the compound has the following structure:  Formula (Ic) – allegedly present in Claim 17 of US'563/PD_1 and R^1, R^2 & R^5 are each independently hydrogen [page 307 of US'563/PD_1] and R^4 is hydrogen [page 309 of US'563/PD_1]
G. Alternative I when G is an amide: R^3 is -A-D-E-G, **[Page 2, line 14]** where A is a bond **[Page 2, line 15]** D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 2, line 24]**, optionally substituted pyrrolidine **[Page 35, line 26]**	***G. Alternative I when G is an amide***: R^3 is -A-D-E-G, where A is a bond [claim 2] D is an optionally substituted (C_2-C_{10}) heterocyclolene [claim 3], and optionally substituted pyrrolidine [Claim 4]

E is a bond **[Page 2, line 25]** G is [-C(O)N(R^a)(R^b)] **[Page 2, lines 32-33]** R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl **[Page 5, lines 15-16]** where the "*optional substituents*" include halogenated (C_1-C_8) alkyl group, i.e., CF_3 **[Page 35, lines 12-13]**.	E is a bond [Claim 5] G is [-C(O)N(R^a)(R^b)] [Claims 6 and 7] R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl where the "optional substituents" are defined on page 44 of US'563/PD_1 as including halogenated (C_1-C_8) alkyl group, i.e., CF_3.
H. Alternative II when E is amide: R^3 is -A-D-E-G, **[Page 2, line 14]** where A is a bond **[Page 2, line 15]** D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 2, line 24]**, optionally substituted pyrrolidine **[Page 35, line 26]** G is CF_3 **[Page 2, line 30, Page 3, line 1]** E is [-C(O)N(R^a)(R^b)] **[missing]]** R^a is H **[Page 5, lines 15-16]** R^e for each occurrence is independently a bond. **[Page 5, line 23]**.	***H. Alternative II when E is amide***: R^3 is -A-D-E-G, where A is a bond [claim 2] D is an optionally substituted (C_2-C_{10}) heterocyclolene [claim 3], optionally substituted pyrrolidine [Claim 4] G is CF_3 E is [-C(O)N(R^a)(R^b)] R^a is H R^e for each occurrence is independently a bond or an optionally substituted (C_1-C_{10}) alkylene.

22. As is self-evident, the text of US'563 of 01.12.2009 referenced by AbbVie to justify the priority claim for Upadacitinib is equally present and practically in the same sequence and in same form in US'604 of 05.12.2008 – which was also filed by Abbott the predecessor in interest of AbbVie.

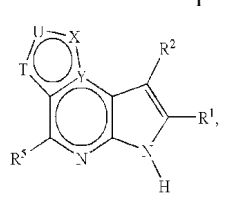
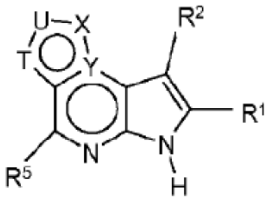
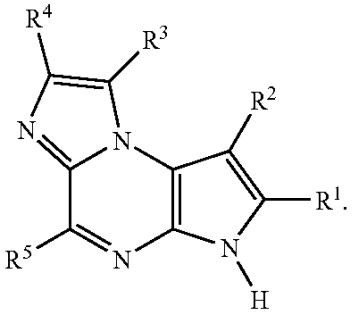
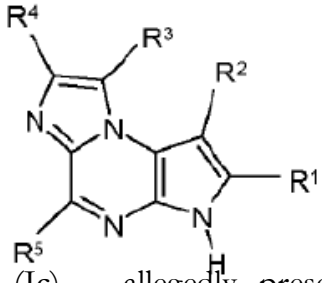
23. This makes it abundantly clear that IN'4759 was not filed within 12 months of an earlier application from which priority could have been claimed, viz., US'604. Thus, on this ground alone, the grant of patent sought on IN'4759 is liable to be refused.

C. WO2009/152133/D1 ::

24. Reliance is now placed on WO2009/0152133 i.e., D1 having a filing date of 09.06.2009. This PCT International Application/Publication

also belongs to AbbVie and corresponds to US'338/D2 referenced and relied on above under Section A. This PCT Application entered India as a national phase viz., IN 195/DELNP/2010 which was later granted as IN292307. Pertinently, the portions providing priority basis for Upadacitinib were deleted in the Indian National Phase from claims but remain in the description.

25. The comparative table below shows how priority could have been claimed from WO'133/D1 but was not so claimed.

WO'133/D1 dated 09.06.2009	US'563 dated 01.12.2009
I. Structure: In a first embodiment the invention provides a compound of Formula (I)  pharmaceutically acceptable salts, …wherein **[Page 2, lines 1-5]**	***I. Structure***:  Formula (I)
J. Substitutions: when T is N, U is CR^4, X is CR^3 and Y is N, **[Page 2, line 11]** then the compound has the following structure:  Formula Ic **[Page 18, lines 13-15]** and R^1, R^2 and R^5 are each independently hydrogen **[Page 2 line 18]** and R^4 is hydrogen **[Page 3, line 27]**.	***J. Substitutions***: when T is N, U is CR^4, X is CR^3 and Y is N, then the compound has the following structure:  Formula (Ic) – allegedly present in Claim 17 of US'563/PD_1 and R^1, R^2 and R^5 are each independently hydrogen [page 307 of US'563/PD_1] and R^4 is hydrogen [page 309 of US'563/PD_1]
K. Alternative I when G is an amide: R^3 is -A-D-E-G, **[Page 2, line 32]** where	***K. Alternative I when G is an amide***: R^3 is -A-D-E-G, where

A is a bond **[Page 2, line 33]** D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 3, line 4, 8]**, optionally substituted pyrrolidine **[Page 21, lines 27, 28, 32]** E is a bond **[Page 3, line 9]** G is [-C(O)N(R^a)(R^b)] **[Page 3, lines 15-16]** R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl **[Page 4, lines 29-30]** where the "*optional substituents*" include halogenated (C_1-C_8) alkyl group, i.e., CF_3 **[Page 62, lines 11-21]**.	A is a bond [claim 2] D is an optionally substituted (C_2-C_{10}) heterocyclolene [claim 3], and optionally substituted pyrrolidine [Claim 4] E is a bond [Claim 5] G is [-C(O)N(R^a)(R^b)] [Claims 6 and 7] R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl where the "optional substituents" are defined on page 44 of US'563/PD_1 as including halogenated (C_1-C_8) alkyl group, i.e., CF_3.
L. Alternative II when E is amide: R^3 is -A-D-E-G, **[Page 2, line 32]** where A is a bond **[Page 2, line 33]** D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 3, line 4, 8]**, optionally substituted pyrrolidine **[Page 21, lines 27, 28, 32]** G is CF_3 **[Page 3, line 15, 17]** E is [-C(O)N(R^a)(R^b)] **[absent]** R^a is H **[Page 2, Para 0033]** R^e for each occurrence is independently a bond or an optionally substituted (C_1-C_{10}) alkylene. **[Page 5, lines 3-4]**.	***L. Alternative II when E is amide***: R^3 is -A-D-E-G, where A is a bond [claim 2] D is an optionally substituted (C_2-C_{10}) heterocyclolene [claim 3], optionally substituted pyrrolidine [Claim 4] G is CF_3 E is [-C(O)N(R^a)(R^b)] R^a is H R^e for each occurrence is independently a bond or an optionally substituted (C_1-C_{10}) alkylene.

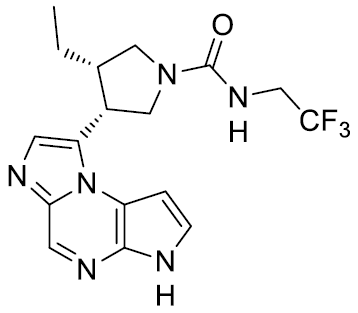
26. As is self-evident, the text of US'563 of 01.12.2009 referenced by AbbVie to justify the priority claim for Upadacitinib is equally present and practically in the same sequence and form in WO'133 of 09.06.2009 – which was also filed by Abbott the predecessor in interest of AbbVie.

27. This makes it abundantly clear that IN'4759 was not filed within 12 months of an earlier application from which priority could have been claimed, viz., WO'133. Thus, on this ground alone, the grant of patent sought on IN'4759 is liable to be refused.

28. WO'133 family, including WO'133, US'338 etc., disclose, and in many jurisdictions claim Upadacitinib. Reference is made here to proceedings on AU2009257602 [**AU'602/D9 to D13**]. For ease of reference, the relevant extracts of AbbVie's submission to the Australian Patent Office while requesting Patent Term Extension due to Patent Office/Regulatory delays in approval are given below.

Letter dated 27.02.2020:

"Upadacitinib is a compound having the structure:

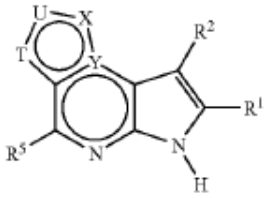


Upadacitinib is a compound of Formula (I) as recited at pages 2 to 2d of the specification, wherein T is N, U is CR4, X is CR3, and Y is N, R1 and R2 are each hydrogen, R5 is hydrogen, R3 is -A-D-E-G, wherein A is a bond, D is optionally substituted pyrrolidinyl, E is -ReC(O)N(Ra)Re-, G is optionally substituted -(C1-C6)alkyl, Ra is a hydrogen, and Re is a bond, R4 is a hydrogen; and the optionally substituted groups are substituted with (C1-C8)alkyl or halogen. The Applicant submits that a specific compound is in substance disclosed in a disclosure of a class of chemical compounds (see Hoffman-La Roche & Co. AG v Commissioner of Patents (1971) CLR 529, applying *Re Mond Nickel Co. Ltd's Application* [1956] RPC 189).

Upadacitinib falls within the scope of at least claims 1 to 4, and 9. The requirements of these claims are met by upadacitinib as follows.

Claim 1

Upadacitinib is a compound of Formula (I)



wherein:

T is N, U is CR4, X is CR3, and Y is N;

R1 and R2 are each hydrogen;

R3 is -A-D-E-G, wherein:

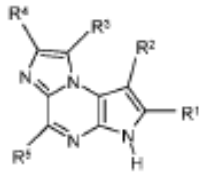
A is a bond;
D is optionally substituted pyrrolidinyl;
E is -ReC(O)N(Ra)Re-;
G is optionally substituted -(C1-C6)alkyl;
Ra is a hydrogen; and
Re is a bond;
R4 is a hydrogen;
R5 is hydrogen; and
the optionally substituted groups are substituted with (C1-C8)alkyl or halogen.

Claim 2
Upadacitinib is a compound of claim 1, wherein E is -ReC(O)N(Ra)Re-.

Claim 3
Upadacitinib is a compound of claim 1 or claim 2, wherein G is optionally substituted -(C1-C6)alkyl.

Claim 4
Upadacitinib is a compound of claims 1 to 3, wherein R1, R2, R4, and R5 are hydrogen.

Claim 9
Upadacitinib is a compound of any one of claims 1 to 6, which is a compound of Formula (Ic):



Formula (Ic)

The date of first inclusion in the ARTG for a good containing, or consisting of, ***a pharmaceutical substance that is in substance disclosed in the specification, and in substance falls within the scope of a claim of the specification, is 17 January 2020****." [emphasis added]*

29. For ease of reference, the relevant provision viz., Section 70(1) to (3) of the Patents Act, 1990 of Australia is reproduced below:

Applications for extension of patent

(1) The patentee of a standard patent may apply to the Commissioner for an extension of the term of the patent if the requirements set out in subsections (2), (3) and (4) are satisfied.

(2) Either or both of the following conditions must be satisfied:

(a) ***one or more pharmaceutical substances per se must in substance be disclosed in the complete specification of the patent and in substance fall within the scope of the claim or claims of that specification****;*

(b) one or more pharmaceutical substances when produced by a process that involves the use of recombinant DNA technology, must in substance be disclosed in the complete specification of the patent and in substance fall within the scope of the claim or claims of that specification.

(3) Both of the following conditions must be satisfied in relation to at least one of those pharmaceutical substances:

(a) goods containing, or consisting of, the substance must be included in the Australian Register of Therapeutic Goods;

(b) the period beginning on the date of the patent and ending on the first regulatory approval date for the substance must be at least 5 years.

30. As is self-evident, this extension on AU2009257602 was possible only if Upadacitinib as a substance ***was in substance disclosed in the complete specification thereof.***

31. In the light of the above, including AbbVie's own admissions before Patent Offices outside India, Upadacitinib is disclsed and claimed in the WO'133 family.

32. MSN therefore submits, that IN'4759 is liable to be rejected in toto as having been filed outside of the 12 months from the earliest application from which priority could have been claimed.

III. Anticipation by prior publication: Section 25(1)(b):

33. Section 25(1)(b)(ii) stipulates that the relevant publication for reliance has to be before the priority date of the impugned claim.

34. It is MSN's case that if the above ground of Section 25(1)(i) is contested by AbbVie and/or considered inapplicable by the Ld. Controller, then equally, IN'4759 is not entitled to the claimed priority date of 01.12.2009 based on US'563.

35. After all, AbbVie cannot have its cake and eat it too – that for purposes of a priority claim, discretely scattered text from US'563 provides a fair basis for the priority claim, but equally present text in earlier patent applications of AbbVie and of the same inventors do not provide such priority-claim basis.

36. In such a case, the only priority forming basis for Claim 1 of IN'4759 is in the text of WO'881 and the priority date has to be taken as the international filing date i.e., 01.12.2010. AbbVie, incidentally, has, through its resounding silence on the European Opposition proceedings and its equally resounding submissions in China, accepted this position.

37. In light of the above, reliance is placed on US'338/D2 published on 17.12.2009. US'338 became US Patent 8962629. Reliance is therefore also placed on US Orange Book Listings i.e., Document D7/OB [a voluntary listing by AbbVie of US patents that according to AbbVie claim Upadacitinib] and also D8/PTE viz., the Patent Term Extension Request filed by AbbVie before the USPTO and D9-13/PTE requests before Australian Patent Office asserting on oath that the respective US and Australian Patents claim Upadacitinib.

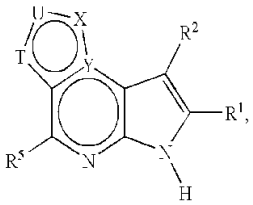
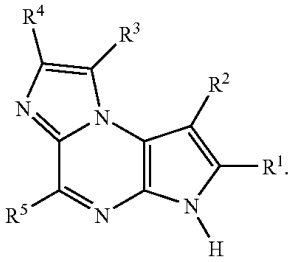
38. Reliance is also placed in this regard on Section 2(1)(l) of The Patents Act, 1970 which provides additional instruction/guidance on how "novelty" i.e., "new invention" must be assessed. This is reproduced hereinbelow with emphasis added for ease of reference:

> *"2(1)(l): "**new invention**" **means any invention or technology** **which has not been anticipated by publication in any document** or used in the country or elsewhere in the world **before the date of filing of patent application with complete specification**, i.e., **the subject matter** has not fallen in public domain or that it **does not form part of the state of the art**;"*

39. It is also settled law that anticipation does not require that the cited document must in express language disclose every tenet of the impugned claim. All that is required is that the single document cited provides the necessary information/disclosure to what is claimed, even if the language

of the impugned claim is not replicated therein. In other words, for anticipating Upadacitinib, it is unnecessary that US'338 give the chemical structure or IUPAC name of Upadacitinib. The only test is whether US'338 contains each essential element of Claim 1 of IN'4759.

40. One set of relevant disclosure from US'338/D2 is extracted below that provides the basis for the claim of anticipation by prior publication.

US'338 dated 09.06.2009
A. Structure: In a first embodiment the invention provides a compound of Formula (I) Formula (I)  pharmaceutically acceptable salts, …wherein **[Page 1, Para 0004]**
B. Substitutions: when T is N, U is CR^4, X is CR^3 and Y is N, **[Page 1, Para 0007]** then the compound has the following structure:  Formula Ic **[Page 12, Para 0174]** and R^1, R^2 and R^5 are each independently hydrogen **[Page 1, Para 0014]** and R^4 is hydrogen **[Page 2, Para 0025]**.
How is Upadacitinib present in US'338: ***I: when G is an amide***: R^3 is -A-D-E-G, **[Page 1, Para 0017]** where A is a bond **[Page 1, Para 0018]** D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 1, Para 0019]**, optionally substituted pyrrolidine **[Page 11, Para 0157]** E is a bond **[Page 1, Para 0020]** G is [-C(O)N(R^a)(R^b)] **[Page 2, Para 0023]** R^a and R^b are independently H, an optionally substituted (C_1-C_{10})alkyl **[Page 2, Para 0033]** where the "*optional substituents*" include halogenated (C_1-C_8) alkyl group, i.e., CF_3 **[Page 33, Para 0369**.

II: when E is amide:

R^3 is -A-D-E-G, **[Page 1, Para 0017]** where
A is a bond **[Page 1, Para 0018]**
D is an optionally substituted (C_2-C_{10}) heterocyclolene **[Page 1, Para 0019]**, optionally substituted pyrrolidine **[Page 11, Para 0157]**
G is CF_3 **[Page 2, Para 0023]**
E is [-C(O)N(R^a)(R^b)] **[Page 1, Para 0020]**
R^a is H **[Page 2, Para 0033]**
R^e for each occurrence is independently a bond or an optionally substituted (C_1-C_{10}) alkylene. **[Page 2, Para 0034]**.

41. The above is just representative. Pertinently, US'338 extensively provides the same list of substitutions for various embodiments, including as preferred embodiments.

42. This position cannot be disputed by AbbVie, in as much as it is AbbVie's admitted position before the USPTO that Upadacitinib is claimed in US'8962629 [patent granted on US'338]. Relevant portions of the Patent Term Extension Request filed by AbbVie before the USPTO are reproduced below for ease of reference:

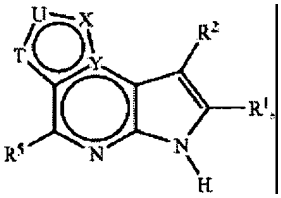
> [***internal page 1***]
> "Pursuant to 35 U.S.C. § 156 and 37 C.F.R. §§ 1.710 to 1.791, AbbVie Inc. ("Applicant" or "AbbVie") herewith applies for an extension of the term of U.S. Patent No. 8,962,629 **(Exhibit 1,** "the '629 patent"). As permitted by 37 C.F.R. § 1.785 and MPEP § 2761, Applicant is concurrently filing a request for patent term extension of U.S. Patent No. RE47,221, based upon the same regulatory review period."
>
> [***internal page 2***]
> "**The approved product that is relevant to this Application is RINVOQ™ (upadacitinib)** extended-release tablets, for oral use, referred to herein as "RINVOQ" or "Approved Product." The Marketing Applicant for RINVOQ is AbbVie Inc., the same entity as Applicant. Accordingly, Applicant relies on its own activities, and that of its predecessors, and affiliates for purposes of this Application For Extension of Patent Term Under 35 U.S.C. § 156."
>
> [***internal page 7***]
> "**(9) A STATEMENT THAT THE PATENT CLAIMS THE APPROVED PRODUCT**, OR A METHOD OF USING OR MANUFACTURING THE APPROVED PRODUCT, AND A SHOWING WHICH LISTS EACH APPLICABLE PATENT CLAIM

AND DEMONSTRATES THE MANNER IN WHICH AT LEAST ONE SUCH PATENT CLAIM READS ON THE APPROVED PRODUCT OR A METHOD OF USING OR MANUFACTURING THE APPROVED PRODUCT:

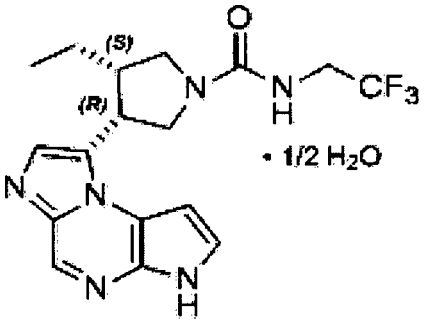
[*internal page 8-12*]
"**The '629 patent claims the Approved Product.** At least claims 1, 4, 11-16, and 28[1] read on the Approved Product. Moreover, at least claims 51 to 53[2] read on methods of using the Approved Product.

Pursuant to 37 C.F.R. § l.740(a)(9), a showing which demonstrates the manner in which at least one patent claim reads on the Approved Product is set forth below.

Claim 1 reads on the Approved Product. That is, claim 1, which is set forth in full in **Exhibit 1,** is directed to compounds of Formula (I):



Formula (I)
As noted in section 1 of this Application, upadacitinib, the active ingredient in RINVOQ has the following structural formula:



See Approved Labeling (Exhibit 3), Section 11 Description.

The structure described as Formula (I) in claim 1 reads on upadacitinib, for example, when:

a) T is N, U is CR4, X is CR[3], and Y is **N;**
b) R[1] and **R[2]** are each hydrogen;
c) R[5] is hydrogen;
d) R[4] is a hydrogen; and
e) R[3] is -A-D-E-G, [3] wherein:

- A is a bond;
- Dis an optionally substituted (C2-C10)heterocyclylene;
- E is —R[e]C(O)N(R[a])R[e]—;[4]
- G is an optionally substituted -(C1-C6)alky1;[5]

a) *R[a]* is a hydrogen; and
b) *Re* is a bond.

When defining the possible substituents for claim 1 as discussed above such that the claim reads on the Approved Product, claims 4, and 13-16 also then read on the Approved Product as discussed further below.

Claim 4, which is dependent on claim 1, reads on the Approved Product when, as discussed above for claim 1, T is N, U is CR4, X is CR3, and Y is N, which forms a compound of Formula (Ie).

Claim 13, which is dependent on claim 1, reads on the Approved Product when R^3 in claims 1 and 13 is -A-D-E-G and A is a bond.

Claim 14, which is dependent on claim 13, reads on the Approved Product when, in addition to the selections noted above for claims 1 and 13, D in claim 1 is an optionally substituted (C2-C10)heterocyclylene, and Din claim 14 is an optionally substituted pyrrolidinyl.

Claim 15, which is dependent on claim 14, reads on the Approved Product when, in addition to the selections noted above for claims 1, 13, and 14, E in claims 1 and 15 is

—R^eC(O)N(R^a)R^e—.

Also, claim 16, which is dependent on claim 15, reads on the Approved Product when, in addition to the selections noted above for claims 1, and 13-15, Gin claims 1 and 16 is optionally substituted (C1-C6)alkyl.

In addition, claims 51 and. 52 read on methods of using the Approved Product and recite as follows:

c) A method of treating or ameliorating a disease or disorder in an individual in need thereof, comprising administering to the individual a compound of claim 1, wherein the disease or disorder is rheumatoid arthritis (RA), psoriasis, juvenile rheumatoid arthritis (JRA), Crohn's disease, psoriatic arthritis, ankylosing spondylitis, or ulcerative colitis.

d) The method of claim 51, wherein disease or disorder is rheumatoid arthritis (RA).

[relevant footnotes reproduced below:]

[1] Claim 11, which is dependent on claim 1, reads on the Approved Product when R^3 in claims 1 and 11 is an optionally substituted (C2-C10)heterocyclyl. The term "heterocyclyl" is defined as "non- aromatic, ring systems, including, but not limited to, monocyclic, bicyclic, tricyclic and spirocyclic rings, which can be completely saturated or which can contain one or more units of unsaturation, for the avoidance of doubt, the degree of unsaturation does not result in an aromatic ring system) and have 5 to 12 atoms including at least one heteroatom, such as nitrogen, oxygen, or sulfur." ('629 patent, 56:51-58).

Claim 12, which is dependent on claim 11, reads on the Approved Product when **R^3** in claims **1** and 11 is an optionally substituted (C2-C

10)heterocyclyl, and R^3 in claim 12 is an optionally substituted pyrrolidinyl.

Claim 28, which is dependent on claim 11, also reads on the Approved Product when, in addition to the selections noted above for claims 1 and 11, R2 and R^5 are each hydrogen.

[2] Claim 53 recites a method of using the Approved Product not currently approved by FDA. It is Applicant's understanding that such a claim nonetheless should be included in the listing of claims pursuant to 37 C.F.R. § 1.740."

[3] Alternatively, as discussed earlier, *supra* note 1, Claims 1, 11, 12, and 28 read on the Approved
Product if R^3 in claim 1 is an optionally substituted (C2-C 10)heterocyclyl (instead of A-D-E-G). The selections for T, U, **X, Y, R**1, R2, **R^4** and R^5 would be the same as defined above.

[4] Alternatively, Claim 1 reads on the Approved Product if Eis a bond, G is -C(O)N(Ra)(Rb), *Ra* is a hydrogen, and *Rb* is an optionally substituted (C1-C10) alkyl. The selections for T, U, **X, Y,** R1, **R^2,** R4, R^5, and R3, A and D would be the same as defined above.

5 Alternatively, Claim 1 reads on the Approved Product if G is CF3, one *Re* is a bond, the other *Re* is an optionally substituted alkylene, Ra is hydrogen, and selections for T, U, **X, Y,** R1, R2, R4, R^5, R3, A, D, and E are as defined above."

43. This is the admitted position of AbbVie and before an authority competent to consider and adjudicate on such position, viz., the USPTO. Given this, IN'4759 claiming solely Upadacitinib has to be rejected.

44. Even if it is considered that [assuming without admitting], that US'338 was published **after the priority date of IN'4759**, it still requires rejection based on Section 2(1)(l) – in terms of which Upadacitinib has already fallen in the public domain and was part of the state of the art before the filing date of IN'4759.

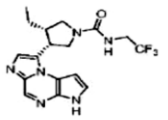
45. Thus, IN'4759 is liable to be refused on this ground alone.

IV. Section 25(1)(e): Sole Claim 1 of IN'4759 clearly does not involve any inventive step/is obvious having regard to matter published as mentioned in clause (b)

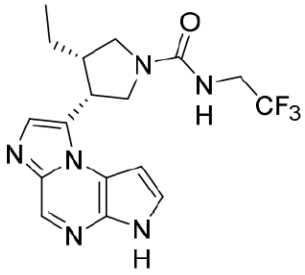
46. While the grounds of lack of inventive step and of obviousness are treated as separate grounds in The Patents Act, 1970, they are being raised in tandem herein since the relevant prior art disclosure relied on for both grounds overlaps. This is not a surrender or admission that the grounds are the same and should be considered as one.

47. It is common ground that Upadacitinib is Compound No. AA.1.160 and was disclosed for the first time in WO2011068881 dated 01/12/2010. The Compound is referenced on page 41 of WO'881 via the IUPAC name. Characterisation of Upadacitinib is given at page 363 of WO'881. The relevant extract is given below:

(3*S*,4*R*)-3-Ethyl-4-(3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazin-8-yl)-pyrrolidine-1-carboxylic acid (2,2,2-trifluoro-ethyl)-amide.

Stereoisomers [Chiral Separation Method]	Structure	Ex. #	R_t min (method)	*m/z* ESI+ $(M+H)^+$
(*cis*)-3-ethyl-4-(3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazin-8-yl)-*N*-(2,2,2-trifluoroethyl)pyrrolidine-1-carboxamide (prepared using **J.1** with Preparation #F.1.1 and 2,2,2-trifluoroethanamine, and **D** with NaOH). [Table 2, Method **69**, R_t = 15.5 min, or = negative]		AA.1.160	1.52 **(a)**	381

48. Upadacitinib has the following:



49. These two grounds of lack of inventive step and obviousness are set out hereinafter in the following sections:

A. Relevant Legal Framework/Applicable Law
B. According to IN'4759, what is the "inventive step" & Relevant portions of the relied-on documents and IN'4759
C. Conclusions.

A. Relevant Legal Framework/Applicable Law :

50. Section 2(1)(ja) defines inventive step in the following manner:

> "*inventive step" means a feature of an invention that involves technical advance as compared to existing knowledge* ***or*** *having economic significance or both that makes the invention not obvious to a person skilled in the art".*

51. Section 10(4) of The Act sets out what is required in a complete specification for a patent application.

> *Every complete specification shall—*
> *(a)fully and particularly describe the invention and its operation or use and the method by which it is to be performed;*
> *(b)disclose the best method of performing the invention which is known to the applicant and for which he is entitled to claim protection; and*
> *(c)end with a claim or claims defining the scope of the invention for which protection is claimed;*
> *(d)be accompanied by an abstract to provide technical information on the invention:*

52. It is settled law that where there is a commonality of inventors and/or applicant-assignee, the standard is higher – the test is no longer just of "skilled in the art" but "person in the know" [*AstraZeneca v. Intas, Delhi High Court, Judgment dated 20.07.2021; SLP preferred by AstraZeneca rejected by Hon'ble Supreme Court*].

53. Reliance is also placed in this regard on Section 2(1)(l) of The Patents Act, 1970 which provides additional instruction/guidance on how "novelty" i.e., "new invention" must be assessed. This is reproduced hereinbelow with emphasis added for ease of reference:

> *"2(1)(l): "****new invention****" ****means any invention or technology which has not been anticipated by publication in any document*** *or used in the country or elsewhere in the world* ***before the date of filing of patent application with complete specification****, i.e.,* ***the subject matter*** *has not fallen in public domain or that it* ***does not form part of the state of the art****;"*

54. Further, any assertion that Upadacitinib is a selection, has to be accompanied by showing that there is basis in IN'4759 as filed to show that this compound performs better, has a technical advancement over the compounds of the prior art, and/or provides some economic significance. Post-filed data is considered irrelevant if, borrowing the words of the Hon'ble High Court of Delhi – "*there is no seed for this information in the complete specification*".

55. This test of "seed in the complete specification" finds acceptance in other jurisdictions based on "plausibility" – such as in the United Kingdom, where, by a recent final Judgment, a second/species application /patent was held invalid on the basis that the specification simply provided no information to show advantages over prior art/genus patent.

56. In the above context, it is relevant that the text in IN'4759 relating to purported assays carried out is practically a straight lift from corresponding portions of US'338.

B. According to IN'4759, what is the "inventive step"

57. IN'4759 in its complete specification states that the objective is to

> *"The invention provides a novel class of compounds, phannaceutical compositions comprising such compounds and methods of using such compounds to treat or prevent diseases or disorders associated with abnomial or deregulated kinase activity, particularly diseases or disorders that involve abnormal activation of the Jakl, Jak2, Jak3, Tyk2, KDR, Flt-3, CDK2, CDK4, TANK, Trk, FAK, Abl, Bcr-Abl, cMet, b-RAF, FGFR3, c-kit, PDGF-R, Syk, BTK, CSFIR, PKC kinases or Aurora kinases" [Section Titled: Background to the Invention]*

58. The purported "Summary of the Invention" has a Markush claim, with a plenitude of substitutions, variations and permutations, and combinations. It is an admitted position that this section provides basis for Upadacitinib when selections are carried out for the various positions in the Markush structure. It is also abundantly clear that there is actually no special feature attached to these specific substitutions as opposed to other substitutions – in other words, IN'4759 is signally silent on any technical advantage attached to the substitutions which lead to Upadacitinib. This silence is with respect to other substitutions leading to other compounds exemplified in IN'4759 and extends equally to the substitutions set out in prior art such as US'338/WO'133 etc.

59. The section titled "*Detailed Description of the Invention*" in IN'4759 merely sets out historical references to JAK inhibition – but fails to set out any problems associated with prior art patents/applications/

publications in this field. In fact, it signally fails to reference any specific prior art patent/application [including their own WO'133/US'338], let alone setting out any technical problems with such prior art and any technical advantages of any compound [forget Upadacitinib] over such prior art compounds.

60. A side-by-side comparison of the respective sections titled "*Detailed Description of the Invention*" is given below. The differences are highlighted.

WO'133/US'338 – Background	IN'4759 – Background
Protein kinases are a broad and diverse class, of over 500 enzymes, that include oncogenes, growth factors receptors, signal transduction intermediates, apoptosis related kinases and cyclin dependent kinases. They are responsible for the transfer of a phosphate group to specific tyrosine, serine or threonine amino acid residues, and are broadly classified as tyrosine and serine/threonine kinases as a result of their Substrate specificity.	Protein kinases are a broad and diverse class, of over 500 enzymes, that include oncogenes, growth factors receptors, signal transduction intermediates, apoptosis related kinases and cyclin dependent kinases. They are responsible for the transfer of a phosphate group to specific tyrosine, serine or threonine amino acid residues, and are broadly classified as tyrosine and serine/threonine kinases as a result of their substrate specificity.
The Jak family kinases (Jak1, Jak2, Jak3 and Tyk2) are cytoplasmic tyrosine kinases that associate with membrane bound cytokine receptors. Cytokine binding to their receptor initiates Jakkinase activation via trans and autophosphorylation processes. The activated Jakkinases phosphorylate residues on the cytokine receptors creating phosphotyrosine binding sites for SH2 domain containing proteins such as Signal Transduction Activators of Transcript (STAT) factors and other signal regulators transduction such as SOCS proteins and SHIP phosphatases.	The Jak family kinases (Jakl, Jak2, Jak3 and Tyk2) are cytoplasmic tyrosine kinases that associate with membrane bound cytokine receptors. Cytokine binding to their receptor initiates Jak kinase activation via trans and autophosphorylation processes. The activated Jak kinases phosphorylate residues on the cytokine receptors creating phosphotyrosine binding sites for SH2 domain containing proteins such as Signal Transduction Activators of Transcript (STAT) factors and other signal regulators transduction such as suppressor of cytokine signaling (SOCS) proteins and SH2 domain-containing inositol 5'-phosphatases (SHIP). **[Note: The difference is only in sentence construction, not in content].**
Activation of STAT factors via this process leads to their dimerization, nuclear translocation and new mRNA transcription	Activation of STAT factors via this process leads to their dimerization, nuclear translocation and new mRNA transcription

resulting in expression of immunocyte proliferation and Survival factors as well as additional cytokines, chemokines and molecules that facilitate cellular trafficking (see Journal of Immunology, 2007, 178, p.2623). Jak kinases transduce signals for many different cytokine families and hence potentially play roles in diseases with widely different pathologies including but not limited to the following examples. Both Jak1 and Jak3 control signaling of the so-called common gamma chain cytokines (IL2, IL4, IL7, IL9, IL 15 and IL21), hence simultaneous inhibition of either Jak1 or Jak3 could be predicted to impact Th1 mediated diseases such as rheumatoid arthritis via blockade of IL2, IL7 and IL15 signaling. On the other hand, IL2 signaling has recently been shown to be essential for development and homeostasis of T-regulatory cells (MalekT R et al., Immunity, 2002, 17(2), p. 167-78). Thus, based on genetic data, blockade of IL2 signaling alone is predicted to result in autoimmunity (Yamanouchi Jet al., Nat. Genet., 2007, 39(3), p. 329-37, and Willerford D M et al., Immunity, 1995, 3(4), p. 521-30). Th2 mediated diseases such as asthma or atopic dermatitis via IL4 and IL9 signaling blockade. Jak1 and Tyk2 mediate signaling of IL13 (see Int. Immunity, 2000, 12, p. 1499). Hence, blockade of these may also be predicted to have a therapeutic effect in asthma. These two kinases are also thought to mediate Type I interferon signaling; their blockade could therefore be predicted to reduce the severity of systemic lupus erythematosus (SLE). Tyk2 and Jak2 mediate signaling of IL12 and IL23. In fact, blockade of these cytokines using monoclonal antibodies has been effective in treating psoriasis. Therefore, blockade of this pathway using inhibitors of these kinases could be predicted to be effective in psoriasis as well. In summary, this invention describes small-molecule compounds that inhibit, regulate and/or modulate Jak family kinase activity that is pivotal to several mechanisms thought	resulting in expression of immunocyte proliferation and survival factors as well as additional cytokines, chemokines and molecules that facilitate cellular trafficking (see *Journal of Immunology,* 2007, 178, p. 2623). Jak kinases transduce signals for many different cytokine families and hence potentially play roles in diseases with widely different pathologies including but not limited to the following examples. Both Jakl and Jak3 control signaling of the so-called common gamma chain cytokines (IL2, IL4, 1L7, IL9, IL15 and 1L21), hence simultaneous inhibition of either Jakl or Jak3 could be predicted to impact Thl mediated diseases such as rheumatoid arthritis via blockade of IL2, IL7 and IL15 signaling. On the other hand, IL2 signaling has recently been shown to be essential for development and homeostasis of T-regulatory cells (Malek TR *et al. Immunity,* **2002,** 17(2), p. 167-78). Thus, based on genetic data, blockade of IL2 signaling alone is predicted to result in autoimmunity (Yamanouchi J *et al, Nat Genet.,* **2007,** 59(3), p.329-37, and Willerford DM *et al.. Immunity,* **1995,** *3(A),* p.521-30). Th2 mediated diseases such as asthma or atopic dermatitis via IL4 and IL9 signaling blockade. Jakl and Tyk2 mediate signaling of IL13 (see Int. Immunity, 2000, 12, p. 1499). Hence, blockade of these may also be predicted to have a therapeutic effect in asthma. These two kinases are also thought to mediate Type I interferon signaling; their blockade could therefore be predicted to reduce the severity of systemic lupus erythematosus (SLE). Tyk2 and Jak2 mediate signaling of IL12 and IL23. In fact, blockade of these cytokines using monoclonal antibodies has been effective in treating psoriasis. Therefore, blockade of this pathway using inhibitors of these kinases could be predicted to be effective in psoriasis as well. In summary, this invention describes small-molecule compounds that inhibit, regulate and/or modulate Jak family kinase activity that is pivotal to several mechanisms thought

critical to the progression of autoimmune diseases including, but not limited to, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), multiple sclerosis (MS), Crohn's disease, psoriasis and asthma.	critical to the progression of autoimmune diseases including, but not limited to, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), multiple sclerosis (MS), Crohn's disease, psoriasis and asthma.

61. The above text is representative of the identity of textual matter under "*Detailed Description of the Invention*" between relied on US'338/WO'133 and IN'4759. The replication is in fact, extensive.

62. On page 53 of IN'4759, AbbVie states as follows:

> *"The studies cited above and others studies confirm the critical role of PKCtheta in T cells activation and in mast cell (MC) signaling. Thus an inhibitor of PKCtheta would be of therapeutic benefit in treating immunological disorders and other diseases mediated by the inappropriate activation of T cells and MC signaling.*
>
> *Many of the kinases, whether a receptor or non-receptor tyrosine kinase or a S/T kinase have been found to be involved in cellular signaling pathways involved in numerous pathogenic conditions, including immunomodulation, inflammation, or proliferative disorders such as cancer.*
>
> *Many autoimmune diseases and disease associated with chronic inflammation, as well as acute responses, have been linked to excessive or unregulated production or activity of one or more cytokines.*
>
> *The compounds of the invention are also useful in the treatment of cardiovascular disorders, such as acute myocardial infarction, acute coronary syndrome, chronic heart failure, myocardial infarction, atherosclerosis, viral myocarditis, cardiac allograft rejection, and sepsis associated cardiac dysfunction. Furthermore, the compounds of the present invention are also useful for the treatment of central nervous system disorders such as meningococcal meningitis, Alzheimer's disease and Parkinson's disease."*

63. Exactly the same text is present in US'338/US'629 in Column 45-46. In fact, it is a given that there is absolute identity of text in the "Detailed Description of the Invention" in terms of combinations, background to Jak inhibitory activity, substitutions, and definitions.

64. What is critical is the fact that there is identity of the manner in which assays are carried out – as set out in US'338/WO'133'US'629 and in IN'4759, with identity of results obtained. These are compared below:

US 2009/0312338	WO 2011/068881
[0399] The use of compounds of the present invention in the manufacture of pharmaceutical compositions is illustrated	The use of compounds of the present invention in the manufacture of pharmaceutical compositions is illustrated

by the following description. In this description the term “active compound” denotes any compound of the invention but particularly any compound which is the final product of one of the following Examples.

a) Capsules

[0400] In the preparation of capsules, 10 parts by weight of active compound and 240 parts by weight of lactose can be de-aggregated and blended. The mixture can be filled into hard gelatin capsules, each capsule containing a unit dose or part of a unit dose of active compound.

b) Tablets

[0401] Tablets can be prepared, for example, from the following ingredients.

Parts by weight

Active compound	10
Lactose	190
Maize starch	22
Polyvinylpyrrolidone	10
Magnesium stearate	3

[0402] The active compound, the lactose and some of the starch can be de-aggregated, blended and the resulting mixture can be granulated with a solution of the polyvinylpyrrolidone in ethanol. The dry granulate can be blended with the magnesium stearate and the rest of the starch. The mixture is then compressed in a tabletting machine to give tablets each containing a unit dose or a part of a unit dose of active compound.

c) Enteric Coated Tablets

[0403] Tablets can be prepared by the method described in (b) above. The tablets can be enteric coated in a conventional manner using a solution of 20% cellulose acetate phthalate and 3% diethyl phthalate in ethanol:dichloromethane (1:1).

d) Suppositories

[0404] In the preparation of suppositories, for example, 100 parts by weight of active compound can be incorporated in 1300 parts by weight of triglyceride suppository base and the mixture formed into

by the following description. In this description the term "active compound" denotes any compound of the invention but particularly any compound which is the final product of one of the following Examples.

a) Capsules

In the preparation of capsules, 10 parts by weight of active compound and 240 parts by weight of lactose can be de-aggregated and blended. The mixture can be filled into hard gelatin capsules, each capsule containing a unit dose or part of a unit dose of active compound.

b) Tablets

Tablets can be prepared, for example, from the following ingredients.

Parts by weight

Active compound	10
Lactose	190
Maize starch	22
Polyvinylpyrrolidone	10
Magnesium stearate	3

The active compound, the lactose and some of the starch can be de-aggregated, blended and the resulting mixture can be granulated with a solution of the polyvinylpyrrolidone in ethanol. The dry granulate can be blended with the magnesium stearate and the rest of the starch. The mixture is then compressed in a tabletting machine to give tablets each containing a unit dose or a part of a unit dose of active compound.

c) Enteric coated tablets

Tablets can be prepared by the method described in (b) above. The tablets can be enteric coated in a conventional manner using a solution of 20% cellulose acetate phthalate and 3% diethyl phthalate in ethanohdichloromethane (1 :1).

d) Suppositories

In the preparation of suppositories, for example, 100 parts by weight of active compound can be incorporated in 1300 parts by weight of triglyceride suppository base and the mixture formed into

suppositories each containing a therapeutically effective amount of active ingredient.	suppositories each containing a therapeutically effective amount of active ingredient.
ASSAYS **In Vitro Jak1 Kinase Activity Measured by Homogenous Time-Resolved Fluorescence (HTRF)** [0504] Purified Jak1 enzyme (aa 845-1142; expressed in SF9 cells as a GST fusion and purified by glutathione affinity chromatography) was mixed with 2 μM peptide substrate (biotin-TYR2, Sequence: Biotin-(Ahx)-AEEEYFFLFA-amide) at varying concentrations of inhibitor in reaction buffer: 50 mM MOPSO pH 6.5, 10 mM $MgCl_2$, 2 mM $MnCl_2$, 2.5 mM DTT, 0.01% BSA, 0.1 mM Na_3VO_4 and 0.001 mM ATP. After about 60 min incubation at room temperature, the reaction was quenched by addition of EDTA (final concentration: 100 mM) and developed by addition of revelation reagents (final approximate concentrations: 30 mM HEPES pH 7.0, 0.06% BSA, 0.006% Tween-20, 0.24 M KF, 80 ng/mL PT66K (europium labeled anti-phosphotyrosine antibody cat #61T66KLB Cisbio, Bedford, Mass.) and 3.12 μg/mL SAXL (Phycolink streptavidin- allophycocyanin acceptor, cat #PJ52S, Prozyme, San Leandro, Calif.). The developed reaction was incubated in the dark either at about 4° C. for about 14 h or for about 60 min at room temperature, then read via a time-resolved fluorescence detector (Rubystar, BMG) using a 337 nm laser for excitation and emission wavelengths of 620 nm and 665 nm. Within the linear range of the assay, the ratio of observed signal at 620 nm and 665 nm is directly related to phosphorylated product and used to calculate the IC_{50} values. [0505] Other kinase assays were performed using a similar protocol. Additional purified enzymes Tyk2 (aa 880-1185 with an N-terminal histidine-tag and C-terminal	**ASSAYS** **In vitro Jakl kinase activity measured by time-resolved fluorescence resonance energy transfer (trFRET)** Varying concentrations of inhibitor were added to an assay well containing: Jakl enzyme (aa 845-1142; expressed in SF9 cells as a GST fusion and purified by glutathione affinity chromatography; 4 nM), peptide substrate (biotin-TYR2, Sequence: Biotin-(Ahx)-AEEEYFFLFA-amide; 2 μM), MOP80 pH 6.5 (50 mM), $MgCl_2$ (10 mM), $MnCl_2$ (2 mM), DTT (2.5 mM), BSA (0.01% w/v), Na_3V0_4 (0.1 mM) and ATP (0.001 mM). After about 60 min incubation at rt, the reaction was quenched by addition of EDTA (final concentration: 100 mM) and developed by addition of revelation reagents (final approximate concentrations: 30 mM HEPES pH 7.0, 0.06% BSA, 0.006% Tween-20, 0.24 M KF, 80 ng/mL PT66K (europium labeled anti-phosphotyrosine antibody cat #61T66KLB Cisbio, Bedford, MA) and 3.12 μg/mL SAXL (Phycolink streptavidin-allophycocyanin acceptor, cat #PJ52S, Prozyme, San Leandro, CA). The developed reaction was incubated in the dark either at about 4 °C for about 14 h or for about 60 min at rt, then read via a time-resolved fluorescence detector (Rubystar, BMG) using a 337 nm laser for excitation and emission wavelength of 665 nm. Within the linear range of the assay, the observed signal at 665 nm is directly related to phosphorylated product and used to calculate the IC_{50} values. **Other in vitro kinase assays measured by time-resolved fluorescence resonance energy transfer (trFRET)** Other kinase assays were performed using a similar protocol. Additional purified enzymes Tyk2 (aa 880-1185 with an N-terminal histidine-tag and C-terminal

FLAG tag; purified in-house by immobilized metal ion affinity chromatography), RET (aa 711-1072 with an N-terminal histidine-tag; purified by immobilized metal ion affinity chromatography) and KDR (aa 792-1354 with an N-terminal histidine-tag; purified in-house by immobilized metal ion affinity and ion-exchange chromatography) were expressed in SF9 cells and Aurora 1/B (aa1-344 with a N-terminal histidine-tag and purified by immobilized metal ion affinity chromatography) was expressed in *E. coli*. Other enzymes used are available from commercial sources. Enzymes were mixed with biotinylated substrates at varying concentrations of inhibitor in different reaction buffers (see Table 1). After about 60 min incubation at room temperature, the reaction was quenched by addition of EDTA and developed by addition of revelation reagents (final approximate concentrations: 30 mM HEPES pH 7.0, 0.06% BSA, 0.006% Tween-20, 0.24 M KF, varying amounts of donor europium labeled antibodies and acceptor streptavidin labeled allophycocyanin (SAXL)). The developed reactions were incubated in the dark at about 4° C. for about 14 h or for about 60 min at room temperature, then read in a time-resolved fluorescence detector (Rubystar, BMG Labtech) as described above.	FLAG tag; purified in-house by immobilized metal ion affinity chromatography), RET (aa 711-1072 with an N-terminal histidine-tag; purified by immobilized metal ion affinity chromatography), Syk (aa356-635 with a C-terminal histidine tag; purified by immobilized metal ion affinity chromatography), and KDR (aa 792-1354 with an N-terminal histidine-tag; purified in-house by immobilized metal ion affinity and ion-exchange chromatography) were expressed in SF9 cells and Aurora 1/B (aal-344 with a N-terminal histidine-tag and purified by immobilized metal ion affinity chromatography) was expressed in E. coli. Other enzymes used are available from commercial sources. Enzymes were mixed with biotinylated substrates at varying concentrations of inhibitor in different reaction buffers (see Table A). After about 60 min incubation at rt, the reaction was quenched by addition of EDTA and developed by addition of revelation reagents (final approximate concentrations: 30 mM HEPES pH 7.0, 0.06% BSA, 0.006% Tween-20, 0.24 M KF, varying amounts of donor europium labeled antibodies and acceptor streptavidin labeled allophycocyanin (SAXL)). The developed reactions were incubated in the dark either at about 4 °C for about 14 h or for about 60 min at rt, then read in a time-resolved fluorescence detector (Rubystar, BMG Labtech) as described above.

The highlight is only to emphasise the identity of mode of assay protocols. The identity of results is set out below:

US'338/WO'133/US'629

Table 1. Specific conditions (per 40 µL enzyme reaction) for the various enzymes are detailed below:

Enzyme	Construct	Substrate	Assay Buffer	Enzyme Conc. (ng/well)	Substrate Conc.	ATP Conc. (mM)	DMSO Conc. (%)	Reaction Time (min)	Detection condition
Jak1	aa 845-1142	Biotin-TYR2	MOPSO	5	2 uM	0.001	5	60	8 ng/well PT66K, 0.39 ug/well SAXL
Jak2	Millipore cat# 14-640	Biotin-TYR1	MOPSO	2.5	2 uM	0.001	5	60	8 ng/well PT66K, 0.078 ug/well SAXL
Jak3	Millipore cat# 14-629	Biotin-TYR2	MOPSO	1	2 uM	0.001	5	60	8 ng/well PT66K, 0.078 ug/well SAXL
Tyk2	aa880-1185	Biotin-TYR1	MOPSO	9	2 uM	0.001	5	60	8 ng/well PT66K, 0.078 ug/well SAXL

IN'4759:

Table A. Specific conditions (per 40 µL enzyme reaction) for the various enzymes are detailed below:

Enzyme	Construct	Substrate	Assay Buffer	Enzyme Conc. (ng/well)	Substrate Conc.	ATP Conc. (mM)	DMSO Conc. (%)	Reaction Time (min)	Detection condition
Jak1	aa 845-1142	Biotin-TYR2	MOPSO	5	2 µM	0.001	5	60	8 ng/well PT66K, 0.39 µg/well SAXL
Jak2	Millipore cat# 14-640	Biotin-TYR1	MOPSO	2.5	2 µM	0.001	5	60	8 ng/well PT66K, 0.078 µg/well SAXL
Jak3	aa 811-1103	Biotin-TYR2	MOPSO	4.5	2 µM	0.001	5	60	8 ng/well PT66K, 0.078 µg/well SAXL
Tyk2	aa880-1185	Biotin-TYR1	MOPSO	9	2 µM	0.001	5	60	8 ng/well PT66K, 0.078 µg/well SAXL

65. Equally, the reaction schemes of both IN'4759, including modes of preparation, reaction conditions, reactants/reagents mirror those of US'338/US'629. Some examples are given below:

Scheme I of US'338 is identical to/mirrored in Scheme I of IN'4759. A listing of the identity of the compounds used and made, and reaction steps is given below. The relevant text portion is Paragraph 0535 of US'338 and Page 91-93 of IN'4759:

Scheme I of US'338	**=**	**Scheme I of IN'4759**:
Compound 8	=	Compound 1
Reaction Condition g	=	Reaction Condition a
Compound 9	=	Compound 2
Reaction Condition h	=	Reaction Condition b
Compound 2	=	Compound 3
Reaction Condition b	=	Reaction Condition c
Compound 3	=	Compound 4
Reaction Condition c	=	Reaction Condition d
Compound 4	=	Compound 5
Reaction Condition d	=	Reaction Condition e
Compound 5	=	Compound 6
Reaction Condition e	=	Reaction Condition f
Compound 6	=	Compound 7
Reaction Condition f	=	Reaction Condition g
Compound 7	=	Compound 8.

Scheme III of US'338 is identical to/mirrored in Scheme II of IN'4759. A listing of the identity of the compounds used and made, and reaction steps is given below. The relevant text portion is Paragraph 0538 of US'338 and Page 93-85 of IN'4759:

Scheme III of US'338	**=**	**Scheme II of IN'4759**:
Compound 2	=	Compound 3
Reaction Condition a	=	Reaction Condition b+c
Compound 11	=	Compound 9
Reaction Condition e	=	Reaction Condition d
Compound 15	=	Compound 12
Reaction Condition f	=	Reaction Condition e+f
Compound 16	=	Compound 14
Reaction Condition g	=	Reaction Condition g

66. The above are just exemplars of the textual identity. These are found across the various schemes present in both specifications.

67. The above identity of assays, results, tableting and other dosage formulation preparation is also accompanied by identity of preparation methods. For brevity, each example is not compared side by side, and

leave is sought to read out the preparation schemes and methods from both texts to show identity. For ease of reference, the Complete Specification of IN'4759 has been highlighted in various sections to show identity with the text of US'338 and where humanly possible, given the constraints of time, relevant paragraphs of US'338 are identified in boxed comments against each section of the corresponding IN'4759 text. Again – this is non-limiting. A reading of IN'4759 leaves no doubt that it is largely a straight lift from US'338.

68. Critically, and this is relevant to obviousness, lack of inventive step, as well as lack of patentable invention grounds, the dosages as set out, including purported combinations with other active ingredients are also identical. Even the animal testing protocols, including reagents, and the number of Lewis rats for example tested [including their gender] are identical.

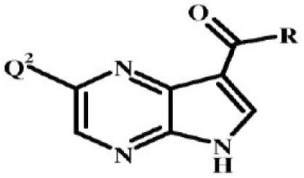
69. What is signally absent – is any showing anywhere in the description that there is in fact any activity associated with Upadacitinib, let alone a therapeutic activity, or any advantage over the compounds of US'338/WO'133 – let alone a significant enhancement in therapeutic efficacy [or any enhancement for that matter]. Simply put, IN'4759 lacks any reference of any advantage of Upadacitinib [let alone any other compound covered by the original Markush structure or of any example thereof] over the compounds of US'338. Pertinently, even compounds overlap. For example, the compound in Example 17, step E of US'338 [Paragraph 976-977] is reproduced in Preparation B on page 215 of IN'4759. Likewise, Example 10 Step D [Paragraph 0861] is reproduced at Preparation MMI of IN'4759 at page 389.

70. Quite apart from WO'133/US'338 reliance is also placed on the following additional information already available in the prior art as of the date of filing or for that matter the claimed priority date of IN'4759. The documents in question are

a. WO/2009/106442 published on 03.09.2009 i.e., D11
b. Kremer et al i.e., Document D12 published July 2009
c. Williams et al, i.e., Document D13 published January 2009

WO'442/D11:

71. WO'442 discloses pyrrolopyrazines of the following structure:



I

72. WO'442 states that the moiety Q2 can be a heteroaryl which in turn may be optionally substituted with one or more Q2a. This moiety Q2a is defined as including Q2b or Q2c.

73. WO'442 further states that when Q2a is Q2c, it can in turn be Q2d or Q2e, and further when Q2e is Q2e', it can be a cycloalkyl optionally substituted with one or more Q2f. WO'442 states that Q2f can be Q2g, which in turn can be C(=O)(Q2h) where in turn Q2h can be amino optionally substituted with one or more Q2i. WO'442 states that Q2i can be a lower haloalkyl.

74. In essence, when this series of substitutions are done, what results is a compound in WO'442 which has a core pyrrolopyrazine which with these substitutions provides an imidazole moiety having a pyrrolidine substituted with amide substituted with a haloalkyl. By definition, a haloalkyl includes a trifluoroethyl.

75. WO'442 discloses, and in fact expressly guides towards pyrazinopyrrole attached to imidazoline ring with a bond and a heterocyclic alkyl group attached to amide group and which in turn is attached to haloalkyl group. It is also trite that pyrrolopyridine is with a pyrrolopyrazine core.

76. The above disclosure provides guidance to a person of skill in the art not just towards as a pointer, but actually directly to create Upadacitinib. Pertinently, pyrrolopyrazine kinase inhibitors of WO'442 are JAK and SYK inhibitors, specifically selectively for inhibition of JAK3, and for treating autoimmune and inflammatory diseases

Kremer et al: Published July 2009

77. The teaching of this document appears to have been extensively explained in an earlier pre-grant opposition which is pending on IN'4759. For purposes of brevity, the following are re-emphasised herein.

78. Kremer et al. teaches the use of an JAK inhibitor viz., labelled CP-690550 in treatment of rheumatoid arthritis. Kremer expressly notes that JAK-3 is critical for signal transduction from the common-chain of the receptors for interleukin-2 (IL2), IL-4, IL- 7, IL-9, IL-15, and IL-21 on the plasma membrane to the nuclei of immune cells and further that these interleukins are integral to lymphocyte activation, function, and proliferation. Kremer further stipulates that JAK-3 is predominantly expressed in cells of the immune system. Ergo, agents that selectively inhibit JAK-3 have potential to mediate potent immune modulation, affecting T lymphocytes, B lymphocytes, macrophages, and NK cells, without significantly affecting other organ systems. [P. 1896, middle paragraph in left column].

Williams et al: Published Jan. 2009

79. Williams et al, is also dealt with extensively in other pre-grant oppositions. For purposes of brevity, reliance is placed on such submissions. The specific portion which is included hereinbelow is only for emphasis.

80. Williams et. al. informs a reader of the growing knowledge in the field that each member of the JAK family has an individual role in the oncogenesis and pathology of the immune system, and that targeting a

conserved ATP-binding site of each specific JAK is one approach to drug design.

81. Williams et al discloses the crystal structure of the JAK2 PTK domain in complex with a pan-JAK inhibitor, 2-t-butyl-9-fluoro-3,6-dihydro-7H-benz[h]-imidaz[4,5-f]isoquinoline-7-one37 (CMP6) developed by Merck.

82. Williams further teaches that fragment-based lead-identification coupled with crystallography was already being used to design potent JAK2 inhibitors.

83. The authors of Williams et al address the challenges of development of specific inhibitors for each Jak member first determining crystal structures of JAK1 PTK domain in complex with two JAK-specific inhibitors, CMP6 and CP-690,550, to 2.0 and 1.9 Å, respectively, as well as the JAK2 PTK domain in complex with CP-690,550 to 2.4 Å resolution. Collectively, these structural data complement the knowledge of this important class of PTKs and provide an invaluable tool for future structure-based development of novel, potent and specific therapeutics against the JAK family.

84. Williams et. al. report the high-resolution crystal structures of the "active form" of the JAK1 PTK domain in complex with two JAK inhibitors, a tetracyclic pyridone 2-t-butyl-9-fluoro-3,6-dihydro-7H-benz[h]-imidaz[4,5-f]isoquinoline-7-one (CMP6) and (3R,4R)-3-[4-methyl-3-[N-methyl-N-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino] piperidin-1-yl]-3-oxopropionitrile (CP-690,550), and compare them with the corresponding JAK2 PTK inhibitor complexes. Both inhibitors bound in a similar manner to JAK1, namely buried deep within a constricted ATP-binding site, thereby providing a basis for the potent inhibition of JAK1. As expected, the mode of inhibitor binding in JAK1 was very similar to that observed in JAK2, highlighting the challenges in developing

JAK-specific inhibitors that target the ATP-binding site. Nevertheless, differences surrounding the JAK1 and JAK2 ATP-binding sites were apparent, thereby providing a platform for the rational design of JAK2- and JAK1-specific inhibitors.

85. In this background, and given the wealth of material information already available, it was incumbent on AbbVie to at the very least set out exactly how Upadacitinib provides any advantage, technical or in terms of therapeutic efficacy, or at the very least the challenges faced with compounds of the art, including those covered and claimed via WO'133/US'338.

86. In this context, US'338/WO'133 discloses that Jak kinases transduce signals for different cytokine families and play a role in diseases with widely different pathologies. WO'133 further discloses that both Jakl and Jak3 control signalling of the so-called common gamma chain cytokines (IL2, IL4, IL7, IL9, IL15 and IL21), hence simultaneous inhibition of either Jakl or Jak3 could be predicted to impact ThI mediated diseases such as rheumatoid arthritis via blockade of IL2, IL7 and IL 15 signalling. Moreover, several pathologically significant cytokines signal via Jakl alone and blockade of one of these, IL6, using an IL6R neutralizing antibody, is shown to significantly improve disease scores in human rheumatoid arthritis patients. Similarly, blockade of GCSF signalling, [also mediated by Jakl alone], using neutralizing monoclonal antibodies or target gene deletion protects mice from experimental arthritis.

87. WO'133/US'338 teaches small molecules for inhibition and modulation of signal transduction of kinases such as Jakl, to treat autoimmune diseases or any other diseases factored on aberrant Jakl function such as rheumatoid arthritis. WO'133/US'338 also teaches in one embodiment that compounds with an improved safety profile are preferred particularly those which selectively avoid inhibition of Jak2.

88. The following specific teaching of US'338/WO'133 is relevant.

> Headgroup Structure: imidazopyrrolopyrazine [two of the general formulae (Ib) and (Ic) , the latter being the basis for priority claim according to AbbVie, are both imidazopyrrolopyrazine headgroups. This, thus would be an obvious place to start for a person of skill in the art.
> Common Substituent on headgroup: either a cycloalkyl ring or a heterocyclic ring.
> When a heterocyclic ring, it is either a pyrrole or a pyrazine ring. [Examples I.1.5, I.1.7, L.3.6, N.1.13, N.1.15, etc., show that use of pyrrole ring is an obvious to try aspect]
> Substituent on heterocyclic ring when a pyrrole: is preferably an alkyl or a substituent connected to the heterocyclic ring via a bridge of either carbonyl or amide. The alkyl is either methyl or ethyl. The substituent is joined to the heterocyclic group via carbonyl or amide is either a cycloalkyl group i.e., cyclopropyl methyl nitrile and methyl - CF3. In effect, it would be obvious for a person of skill in the art to try nitrile and -CF3 as substituents on the amide or carbonyl bridge.

89. MSN therefore submits that WO'133/US'338 expressly teaches preparation of JAK inhibitors with high specificity for JAK1 and have a higher safety profile by avoiding JAK2 inhibition. Williams et al and Kremer et al relied on previously teach detailed structure including the specific amino acid residues present in binding sites of JAK1, JAK2. These documents also teach in detail how different inhibitors interact with the various amino acid residues in the binding sites of different JAKs.

C. Conclusions

90. In this background, a person skilled in the art would find it obvious to try, have sufficient motivation to read and to try the head group of US'338 while attempting to design compounds for Jak inhibition and in particular for treatment of autoimmune diseases, including rheumatoid arthritis or ulcerative colitis.

91. Absent any information in IN'4759 which sets out any advantages of [let alone any problems in], there is no gainsaying that what is provided in the prior art, i.e., the existing art as of the filing date of IN'4759 renders what is claimed therein obvious and also separately lacking in inventive

step. For this reason alone, IN'4759 requires rejection based on the submissions above.

V. Section 25(1)(f) – not an invention or not a patentable invention

92. For the purposes of this ground, reliance is placed inter alia on section 3(d) of The Patents Act, 1970, which is reproduced below for ease of reference.

> "*the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.*
> *Explanation—For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy;*".

93. AbbVie states in its reply to the First Examination Report issued on IN'4759 as well as in its replies to various pre-grant oppositions in India and in an opposition in Europe, that the alleged invention resides in providing compounds which have high potency of inhibition of JAK1 and low potency of inhibition of JAK 2 which results in said compounds possessing better safety profile and higher therapeutic index when used for treatment of diseases mediated by JAK 1 (and JAK3) such as rheumatoid arthritis. At present, this "compound" is only Upadacitinib.

94. WO'133'/US'338 teaches compounds with high affinity for JAK 1 and JAK 3 but low affinity for JAK 2. Some of the disclosure is referenced below:

- line 8-10 on page 47
- Line 34 to 37 on page 45 and lines 1 to 9, 12-15 on page 46
- page 82 which teaches the use of the compounds therein for effect in rheumatoid arthritis
- the entire section relating to preparation of compounds, dosages, activity and co-treatment with other active ingredients; apart from background on Jak inhibition.

95. Thus, what is clear abundantly is that the purported therapeutic efficacy of Upadacitinib is clearly disclosed as also applicable and available from the compounds of WO'133/US'338. AbbVie admits that the closest structural compound to Upadacitinib in WO'133/US'338 is Example 19.

96. That apart, several of the compounds otherwise disclosed in IN'4759 and those of WO'133/US'338 bear close structural similarity as can be seen from bare reading of the two documents.

97. In this background, it was incumbent on AbbVie to set out exactly what advantages in terms of enhanced therapeutic efficacy are provided by Upadacitinib over the compounds of WO'133/US'338, and in particular Example 19. This data is completely absent – and cannot be filled in through post-filed data. There is silence in IN'4759 either data of inhibition of JAK 1 or data of inhibition of JAK 2. There is no data to demonstrate the alleged technical solution of higher affinity for JAK 1 and lower affinity for JAK2 or any comparative data to show enhanced therapeutic efficacy over known compounds including the compound given as Example 19 of D4.

98. Given the identity of preparation methods, identity of results, identity of assay results, identity including of compounds, clearly, Upadacitinib is a derivative of the tricyclic compounds of US'338 – with no information of any advancement of efficacy, let alone a significant advancement of therapeutic efficacy thereof.

99. In the light of the above, IN'4759 is liable to be refused on this ground alone.

VI. Section 25(1)(g): insufficient disclosure

100. If AbbVie contends that the challenge of "out of priority claim" or anticipation by prior publication do not stand established on the basis that the documents relied on do not provide guidance towards Upadacitinib,

then equally, what is now claimed in IN'4759 also lacks sufficient basis in the written description.

101. Claim 1 for Upadacitinib lacks support in terms of The Act since the complete specification does not disclose what is claimed as an invention in a manner where a person of average skill in the art can carry out the invention without undue experimentation.

102. IN'4759 provides information about over-broad synthesis schemes for some compounds. Specific synthesis is given only for around 40 of the compounds. Pertinently, there is no information as to how Upadacitinib [or for that matter its' pharmaceutically acceptable salt] can be prepared. Pertinently, again, none of the 40 compounds whose synthesis is provided are structurally close to Upadacitinib.

103. The general synthesis schemes and procedures provided in IN'4759 even with respect to Upadacitinib do not enable or provide a person of average skill in the art as to what is to be used to prepare Upadacitinib and what process parameters or conditions are relevant. IN'4759 at its very best is no more than an overbroad guide – and a person of average skill has to find a person of inventive ingenuity to find out how to make Upadacitinib, pertinently also – why choose Upadacitinib, and then determine its activity/relevance/use as a therapeutic candidate.

104. The general procedure, particularly Procedure J.1, has no information as to:

- which amine or amine salt is to be used or why a specific amine or amine salt is to be used;
- the optimal reaction time or other reaction conditions qua Upadacitinib.
- which solvent or solvents are to be used.

105. The process of preparation stated for Upadacitinib has gaps which, simply cannot be filled in by a person of skill in the art without extensive experimentation. Thus, IN'4759 fails to disclose the claimed invention fully and sufficiently so as to enable a person of ordinary skill in the art to arrive at the claimed invention without facing the burden of undue experimentation.

106. It is therefore submitted that IN'4759 is liable to be rejected on this ground alone.

VII. Section 8 requirements not met:

107. AbbVie failed to disclose to the Patent Office the information required under Section 8. The Applicant is required to provide all the information regarding the prosecution of the equivalent applications till the grant of the Indian application to the Patent Office in writing from time to time and also within the prescribed time.

108. Specifically, AbbVie even as it amended the claims on IN'292307 to exclude Upadacitinib, failed to inform the IPO that the corresponding US Patent viz., US8962629 claimed Upadacitinib. The inference is obvious – this is deliberate and conscious and to avoid any rejection. The deletion of Upadacitinib forming substitutions from IN'292307 leads to a position in law of disclosure dedication via disclaimer. The failure to inform the Ld. Controller of the family of IN'292307 which includes US'338/US'629 is deliberate – and intended to avoid refusal.

109. AbbVie did not inform the Patent Office of the refusal of Upadacitinib specific claims in China on the ground of lack of inventive step – and after a rejection of any priority claim for Upadacitinib.

110. Pertinently, reports suggest that AbbVie did not even contest the findings of no-priority for Upadacitinib specific claims in either China or Europe – something deliberately concealed from the IPO.

111. Clearly, this was a conscious and deliberate concealment of material information – given that The Patents Act, 1970 has specific provisions for rejection of an application if it is not filed within 12 months of the earliest claimable priority date.

112. MSN will provide further submissions and evidence in this respect once a full family review of AbbVie's patents covering Upadacitinib are available.

CONCLUSION

113. In view of the above, the claimed subject matter is not inventive, non-patentable and the impugned specification is insufficient. The pre-grant opposition as filed may be allowed and the subject patent application may be refused.

HEARING REQUESTED

114. MSN hereby requests a hearing under section 25(1) of the Patents Act, 1970 (hereinafter referred to as "the Patents Act") and Rule 55 of the Patents Rules (hereinafter referred to as "the Rules").

P R A Y E R

In the fact and circumstances of the case, the Opponent prays as follows:

i. that the Controller take the present Opposition on record; that the Indian application 4759/DELNP/2012, be rejected under Section 25(1) of the Patents (Amendment) Act, 2005;

ii. that it be permitted to file further documents and evidence if necessary to support their averments;

iii. that it be permitted to file rejoinder and affidavit if necessary to support their averments;

iv. that it be granted an opportunity of being heard in the matter before any final orders are passed;

v. that it be allowed to make further submissions in case the Applicant makes any amendments in the claims;

vi. any other reliefs considering the facts and circumstances may be granted in favour of MSN and against AbbVie in the interest of justice.

Dated this day of 22nd day of August, 2025.

G. Nataraj
D/536/1993
Advocate for Opponent
MSN Laboratories Pvt. Ltd.
Opponent

To,
The Controller of Patents
The Patent Office, Delhi