Patent infringement risk search (Chem 2022)

Your company is proposing to launch a compound for the treatment of Alzheimers disease in January 2023. Unfortunately, at present the brief from R&D is very broad.

The lead candidates for this launch are all either 2-Piperidinone or Piperidine based molecules that also include a Tetrazole ring structure in another part of the molecule. The compounds of the present invention selectively attenuate A-beta (1-42) production by inhibiting gamma-secretase with a reduced propensity for undesirable side effects.

It is intended to roll-out this change across all its existing markets: EU and the US.

Your colleague patent Attorney asked you to conduct an FTO search for any molecules with these chemical features already used for this type of Alzheimer treatment. It has also been agreed at this stage to exclude any structure searches from this request.

"Theoretical Approach"

This is a search to help indicate to an attorney whether any dominating rights on the indication and/or the compound exists.

Such rights may vary from jurisdiction to jurisdiction and depend on the status of the application/patent in the individual countries.

Focus should be on patents/applications only

The first thing to do with such a search is therefore to define the concepts, in this case the proposed project consists of

- the compound,
- the treatment of Alzheimer by attenuation of A-beta (1-42) production,
- the target gamma-secretase

The approach should address legal status of patents and limits in jurisdiction, and time restrictions which may preferentially be handled after the initial searches are done. Bare in mind that SPC/PTE/PTA may apply.

Relevant further questions, e.g. on analyses of simple family/individual members to the search should be addressed to the attorney.

The use of proximity and wildcard operators as well as synonyms and broader terms should be addressed.

At least a couple of databases should be used of which one would be a full text database and one would be a databased based on indexing.

Searching in fields in full text databases with machine translated text is preferred.

Extend the searching in claims to title and abstracts to raise recall.

The use of classification codes may be an option, particularly on the target and the disease, however, they lack some granularity in chemistry.

"Practical Approach"

1. Value add abstract (patent) database(s)

File WPINDEX on STNext

```
=> S ".gamma.-secretase" OR "gamma-secretase" OR "gamma-secretases" OR
".gamma.-secretases"
       "I-SECRETASE" OR "GAMMA-SECRETASE" OR "GAMMA-SECRETASES" OR
        "Γ-SECRETASES"
=> S ((?secretase?) /CLM, AB, TI)
       (?SECRETASE?) /CLM, AB, TI
=> s (alzheimer#)/clm,ab,ti)
       (ALZHEIMER#) /CLM, AB, TI
=> s ((piperid!non## OR piperid!n##) /CLM,AB,TI)
        (PIPERID!NON## OR PIPERID!N##) /CLM, AB, TI
=> s (tetrazol## ) /CLM,AB,TI
       (TETRAZOL##) /CLM, AB, TI
L5
=> s 11 and 13 and 14 and 15
            11 and 13 and 14 and 15
                                       [SET 1, i.e. retrieve from this
L6
                                       Answer SET additional keywords,
                                       classification(s)..., d 110]
=> s 12 and 13 and 14 and 15
                                       [SET 2, capture overarching
          12 and 13 and 14 and 15
L7
                                       Infringing patents]
=> s 11 and 14 and 15
           11 and 14 and 15
                                      [SET 3 see SET 2 above]
=> s 12 and 14 and 15
           12 and 14 and 15
                                      [SET 4 see SET 2 above]
=> s 13 and 14 and 15
L10
           13 and 14 and 15
                                      [SET 5 see SET 2 above]
```

=> d 111 1- ti

- L11 ANSWER 2 WPINDEX COPYRIGHT 2022 CLARIVATE on STN TI New 1,2-disubstituted **piperidine** derivatives useful for treatment of e.g. **Alzheimer'**s disease, cerebral amyloid angiopathy, multi-infarct dementia, Down's syndrome, or mild cognitive impairment
- L11 ANSWER 3 WPINDEX COPYRIGHT 2022 CLARIVATE on STN
 TI New diffuorinated **piperidine** compounds are beta-amyloid (142) production inhibitors useful for treatment/prevention e.g.
 Alzheimer's disease, cerebral amyloid angiopathy, multi-infarct dementia, dementia pugilistica and Down syndrome
- L11 ANSWER 4 WPINDEX COPYRIGHT 2022 CLARIVATE on STN TI New **piperidine** derivatives useful for treatment or prevention of disease associated with deposition of beta-amyloid in brain e.g. for treatment of **Alzheimer'**s disease or cerebral amyloid angiopathy
- L11 ANSWER 5 WPINDEX COPYRIGHT 2022 CLARIVATE on STN TI New **piperidine** compounds are amyloid beta(1-42) production inhibitors useful in the treatment or prevention e.g. **Alzheimer's** disease and its related conditions, cerebral amyloid angiopathy and dementia pugilistica
- L11 ANSWER 6 WPINDEX COPYRIGHT 2022 CLARIVATE on STN
 TI New benzoimidazole, -oxazole, and -thiazole derivatives are
 beta-secretase inhibitor used to treat e.g. **Alzheimer'**s disease,
 mild cognitive impairment and Down's syndrome
- L11 ANSWER 7 WPINDEX COPYRIGHT 2022 CLARIVATE on STN TI New heteroaroyl derivatives for preparation of medicament for treatment of e.g. **Alzheimer'**s disease, Down syndrome, Parkinson's disease and Huntingdon's chorea, are prolyl endopeptidase and PEP-like enzyme inhibitors
- L11 ANSWER 8 WPINDEX COPYRIGHT 2022 CLARIVATE on STN TI Composition used for treating neuronal diseases e.g. Alzheimer's disease, Down Syndrome, Parkinson disease, Chorea Huntington comprises glutaminyl cyclase inhibitor

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=> s 17 and prd>19970101

L12 L7 AND PRD>19970101

=> s 18 and prd>19970101

L13 L8 AND PRD>19970101

=> s 19 and prd>19970101

L14 L9 AND PRD>19970101

=> s 110 and prd>19970101

L13 L10 AND PRD>19970101
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- L1/L2 concept can be broadened/extended with synonyms like "Amyloid*", "intermembrane protease" or "protease complex"
- L3 concept can be broadened/extended with synonyms like "neurodegenerat*" and/or IPC classification(s) A61P-025/28
- L4 concept can be broadened/extended with " δ -Valerolactam or delta-Valerolactam", "Azacyclohexane", "penta-methyleneamin...", "Azinane", "Azinanone",...
- Additional combination of queries to reveal other overarching infringing patents like "L1 and L3 and L4", "L1 and L3 and L5",
- If recall is too high, limit by using PN/DS US, EP, AT, BE, DE,.... (all European country codes)
- Make use of other value add patent databases.
 - i.e. CAS/Registry Look up gamma secretase in CAS/Reg, extract patent references and further processing of these results (limiting, exporting results,)

2. Full-text (patent) database(s)

e.g: FAMPAT (ORBIT)

- 1. (+ALZHEIMER+ OR NEURO_DEGENERAT+)/TI/AB/CLMS OR (A61P-025/28)/IPC/CPC [underscore_; will retrieve terms that may be written as one or two words, and will retrieve results where there is a hyphen between terms.
- 2. (+ALZHEIMER+ OR NEURO DEGENERAT+)/DESC/ODES

[When a generic/broad concept for Alzheimer/neurodegeneration is used in the claims, this query covers that broad concept defined in the text of the patent as "alzheimer" or "neurodegenation"]

- 3. (+SECRETASE+ OR (INTER_MEMBRANE+ 2D PROTEASE+) OR (PROTEASE+ 2D COMPLEX+) OR +AMYLOID+)/TI/AB/CLMS
- 4. (+SECRETASE+ OR (INTER_MEMBRANE+ 2D PROTEASE+) OR (PROTEASE+ 2D COMPLEX+) OR +AMYLOID+)/DESC/ODES

[see remark query line 2]

- 5. (+TETRAZOLE+)/TI/AB/CLMS OR (C07D-257/04)/IPC/CPC
- 6. (+PIPERIDIN+ OR +PIPERIDON+ OR AZA_CYCLOHEXAN+ OR PENTA_METHYLENEAMIN+ OR AZINANE+ OR AZINANONE+ OR +VALEROLACTAM+)/TI/AB/CLMS
- 7. ((+PIPERIDIN+ OR +PIPERIDON+ OR AZA_CYCLOHEXAN+ OR PENTA_METHYLENEAMIN+ OR AZINANE+ OR AZINANONE+ OR +VALEROLACTAM+) P (+TETRAZOLE+))/DESC/ODES

 [see remark query line 2, P operator; same paragraph]
- 8. PRD >= 1997
- 9. 1 AND 3 AND 5 AND 6 AND 8
- 10. 2 AND 3 AND 5 AND 6 AND 8
- 11. 1 AND 4 AND 5 AND 6 AND 8
- 12. 2 AND 4 AND 5 AND 6 AND 8
- 13. 1 AND 3 AND 7 AND 8
- 14. 2 AND 3 AND 7 AND 8
- 15. 1 AND 4 AND 7 AND 8
- 16. 2 AND 4 AND 7 AND 8
- 17. 1 AND 5 AND 6 AND 8
- 18. 3 AND 5 AND 6 AND 8
- 19. 2 AND 5 AND 6 AND 8
- 20. 4 AND 5 AND 6 AND 8
- 21. 1 AND 7 AND 8
- 22. 3 AND 7 AND 8
- If recall is too high, limit by using PN/DS US, EP, AT, BE, DE,.... (all European country codes)
- Additional combination of queries to reveal other overarching infringing patents like "2 and 7 and 8", "4 and 7 and 8"

(Out of scope for the exam, but would yield bonus points when used in addition to a concept search)

Structure searching in Registry, Markush searching in Marpat (provided more structural information available)
Sequence searching on target.