Enchanting molecules

By Edigles Guedes

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Abstract. We suggest the use of the molecules (7a'R,8'R)-2'-fluoro-N-methyl-2',3',7',7a',8',9',11',11a'-octahydro-1'H-spiro[oxetane-3,10'-pyrido[3,2,1-de]phenazin]-8'-amine,3-fluoro-N-((S)-1,1,1-trifluoropropan-2-yl)-1,2,3,4-tetrahydroquinolin-8-amine, (2S)-2-((3-fluoro-1,2,3,4-tetrahydroquinolin-8-yl)amino)cyclohexanol and N-butyl-3-fluoro-1,2,3,4-tetrahydroquinolin-8-amine for the fight against numerous diseases, after *in silico* analysis.

Keywords: chemoinformatic and drug discovery.

"Jesus said unto her, I am the resurrection, and the life: he that believeth in me, though he were dead, yet shall he live:"
— John 11:25 (KJV)

1. Introduction

In this paper, we suggest using the molecules below [Figures 1, 2, 3 and 4] to combat countless diseases.

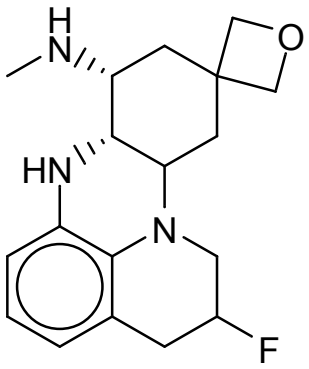

Fig.1. The molecule 1: (7a'R,8'R)-2'-fluoro-N-methyl-2',3',7',7a',8',9',11',11a'-octahydro-1'H-spiro[oxetane-3,10'-pyrido[3,2,1-de]phenazin]-8'-amine ($C_{18}H_{24}FN_3O$).

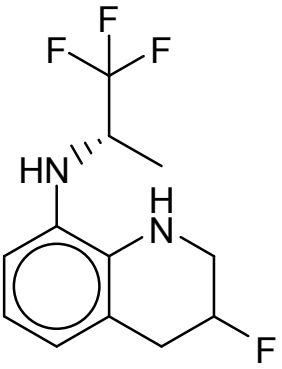

Fig. 2. The molecule 2: 3-fluoro-N-((S)-1,1,1-trifluoropropan-2-yl)-1,2,3,4-tetrahydroquinolin-8-amine ($C_{12}H_{14}F_4N_2$).

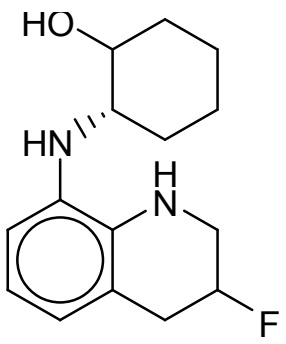

Fig. 3. The molecule 3: (2S)-2-((3-fluoro-1,2,3,4-tetrahydroquinolin-8-yl)amino)cyclohexanol ($C_{15}H_{21}FN_2O$).

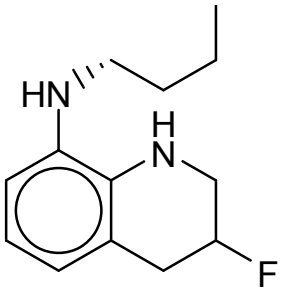

Fig. 4. The molecule 4: N-butyl-3-fluoro-1,2,3,4-tetrahydroquinolin-8-amine ($C_{13}H_{19}FN_2$).

While reading this article, we will show some physicochemical descriptors as well as to predict ADME parameters, pharmacokinetic properties, druglike nature and medicinal chemistry friendliness of the molecule in question, with the help of the SwissADME website, see (Daina et al., 2017),(Daina et al., 2014) and (Daina and Zoete, 2016).Next, we will show the probabilities of the indications of predicted targets, with the help of the Super-PRED (Nickel et al., 2014) website.

Here are some predicted properties of the molecules above:

Molecule 1

SMILES Formula: CN[C@@H]1CC2(COC2)CC3[C@@H]1Nc4cccc5c4N3CC(C5)F
Molecular Formula: $C_{18}H_{24}FN_3O$
Formula Weight: 317.4010632
Composition: C(68.11%) H(7.62%) F(5.99%) N(13.24%) O(5.04%)
Molar Refractivity: 87.10 ± 0.4 cm^3
Molar Volume: 246.3 ± 5.0 cm^3
Parachor: 663.3 ± 6.0 cm^3
Index of Refraction: 1.624 ± 0.03
Surface Tension: 52.5 ± 5.0 dyne/cm
Density: 1.28 ± 0.1 g/cm^3
Polarizability: 34.52 ± 0.5 $10^{-24}cm^3$
RDBE: 8
Monoisotopic Mass: 317.190341 Da
Nominal Mass: 317 Da

Average Mass: 317.4011 Da
M+: 317.189792 Da
M-: 317.190889 Da
[M+H]+: 318.197617 Da
[M+H]-: 318.198714 Da
[M-H]+: 316.181967 Da
[M-H]-: 316.183064 Da.

Molecule 2

SMILES Formula: C[C@@H](C(F)(F)F)Nc1cccc2c1NCC(C2)F
Molecular Formula: $C_{12}H_{14}F_4N_2$
Formula Weight: 262.2465728
Composition: C(54.96%) H(5.38%) F(28.98%) N(10.68%)
Molar Refractivity: 60.21 ± 0.4 cm^3
Molar Volume: 206.6 ± 5.0 cm^3
Parachor: 496.2 ± 6.0 cm^3
Index of Refraction: 1.494 ± 0.03
Surface Tension: 33.2 ± 5.0 dyne/cm
Density: 1.26 ± 0.1 g/cm^3
Polarizability: 23.87 ± 0.5 $10^{-24}cm^3$
RDBE: 5
Monoisotopic Mass: 262.109311 Da
Nominal Mass: 262 Da
Average Mass: 262.2466 Da
M+: 262.108763 Da
M-: 262.10986 Da
[M+H]+: 263.116588 Da
[M+H]-: 263.117685 Da
[M-H]+: 261.100938 Da
[M-H]-: 261.102035 Da.

Molecule 3

SMILES Formula: FC(C1)CNc2c1cccc2N[C@@H]3C(O)CCCC3
Molecular Formula: $C_{15}H_{21}FN_2O$
Formula Weight: 264.3384432
Composition: C(68.16%) H(8.01%) F(7.19%) N(10.60%) O(6.05%)
Molar Refractivity: 73.21 ± 0.4 cm^3
Molar Volume: 219.1 ± 5.0 cm^3
Parachor: 578.2 ± 6.0 cm^3
Index of Refraction: 1.582 ± 0.03
Surface Tension: 48.4 ± 5.0 dyne/cm
Density: 1.20 ± 0.1 g/cm^3
Polarizability: 29.02 ± 0.5 $10^{-24}cm^3$
RDBE: 6
Monoisotopic Mass: 264.163792 Da
Nominal Mass: 264 Da
Average Mass: 264.3384 Da
M+: 264.163243 Da
M-: 264.16434 Da
[M+H]+: 265.171068 Da
[M+H]-: 265.172165 Da
[M-H]+: 263.155418 Da
[M-H]-: 263.156515 Da.

Molecule 4

SMILES Formula: FC(C1)CNc2c1cccc2NCCCC
Molecular Formula: $C_{13}H_{19}FN_2$
Formula Weight: 222.3017632
Composition: C(70.24%) H(8.61%) F(8.55%) N(12.60%)
Molar Refractivity: 64.50 ± 0.4 cm^3
Molar Volume: 206.6 ± 5.0 cm^3
Parachor: 514.6 ± 6.0 cm^3
Index of Refraction: 1.536 ± 0.03
Surface Tension: 38.4 ± 5.0 dyne/cm
Density: 1.07 ± 0.1 g/cm^3
Polarizability: 25.57 ± 0.5 $10^{-24}cm^3$
RDBE: 5
Monoisotopic Mass: 222.153227 Da
Nominal Mass: 222 Da
Average Mass: 222.3018 Da
M+: 222.152678 Da
M-: 222.153775 Da
[M+H]+: 223.160503 Da
[M+H]-: 223.1616 Da
[M-H]+: 221.144853 Da
[M-H]-: 221.14595 Da.

2. Materials and Methods

Through the internet sites and others references (Daina et al., 2017),(Daina et al., 2014), (Daina and Zoete, 2016) and (Nickel et al., 2014), we will study the molecules represented in Figures 1, 2, 3 and 4 above, in order to conclude that it is very promising in the fight against some diseases.

2.1. ADME parameters and others

As seen in Figure 5 and 7, the molecules are lead-likeness, passing through the criteria listed below, as well as having a bioavaliability score of 0.55. As seen in Figures 6 and 8, the molecules are drug-likeness, passing through the criteria listed below, as well as having a bioavaliability score of 0.55. For other information, just look at Annex 1, at the end of this paper.

2.2. The indications of predicted targets

The indication of predicted target for brain cancer is of 94.33% of probability and the model accuracy is of 82.69% of probability, see Fig. 9. The indication of predicted target for multiple sclerosis is of 95.13% of probability and the model accuracy is of 98.95% of probability, see Fig. 10. The indication of predicted target for ocular cancer is of 96.22% of probability and the model accuracy is of 91.11% of probability, see Fig. 11. The indication of predicted target for multiple sclerosis is of 98.71% of probability and the model accuracy is of 98.95% of probability, see Fig. 12. All in Annex 2, at the end of this paper.

3. Results and Discussion

The four molecules are very promising for the fight against some diseases, according to an *in silico* analysis carried out by the SuperPRED website (Nickel et al., 2014), with more than 90% chance of success in the compatibility between the target and the ligand. Besides, the molecules are free of toxicity, as attested by the *in silico* prediction in Annex 1, Figures 5, 6, 7 and 8, all below.

4. Conclusions

In the future, it is possible to do molecular docking, as well as discover new molecules analogous to the one given above.

5. References

Daina, A., Michielin, O., Zoete, V., 2017. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci. Rep. 7, 1–13. https://doi.org/10.1038/srep42717.

Daina, A., Michielin, O., Zoete, V., 2014. iLOGP: A Simple, Robust, and Efficient Description of n-Octanol/Water Partition Coefficient for Drug Design Using the GB/SA Approach | Journal of Chemical Information and Modeling. J. Chem. Inf. Model. 54, 3284–3301. https://doi.org/10.1021/ci500467k.

Daina, A., Zoete, V., 2016. A BOILED-Egg To Predict Gastrointestinal Absorption and Brain Penetration of Small Molecules. ChemMedChem 11, 1117–1121. https://doi.org/10.1002/cmdc.201600182.

Nickel, J., Gohlke, B.-O., Erehman, J., Banerjee, P., Rong, W.W., Goede, A., Dunkel, M., Preissner, R., 2014. SuperPred: update on drug classification and target prediction. Nucleic Acids Res. 42, W26–W31. https://doi.org/10.1093/nar/gku477.

6. Annexs

Annex 1

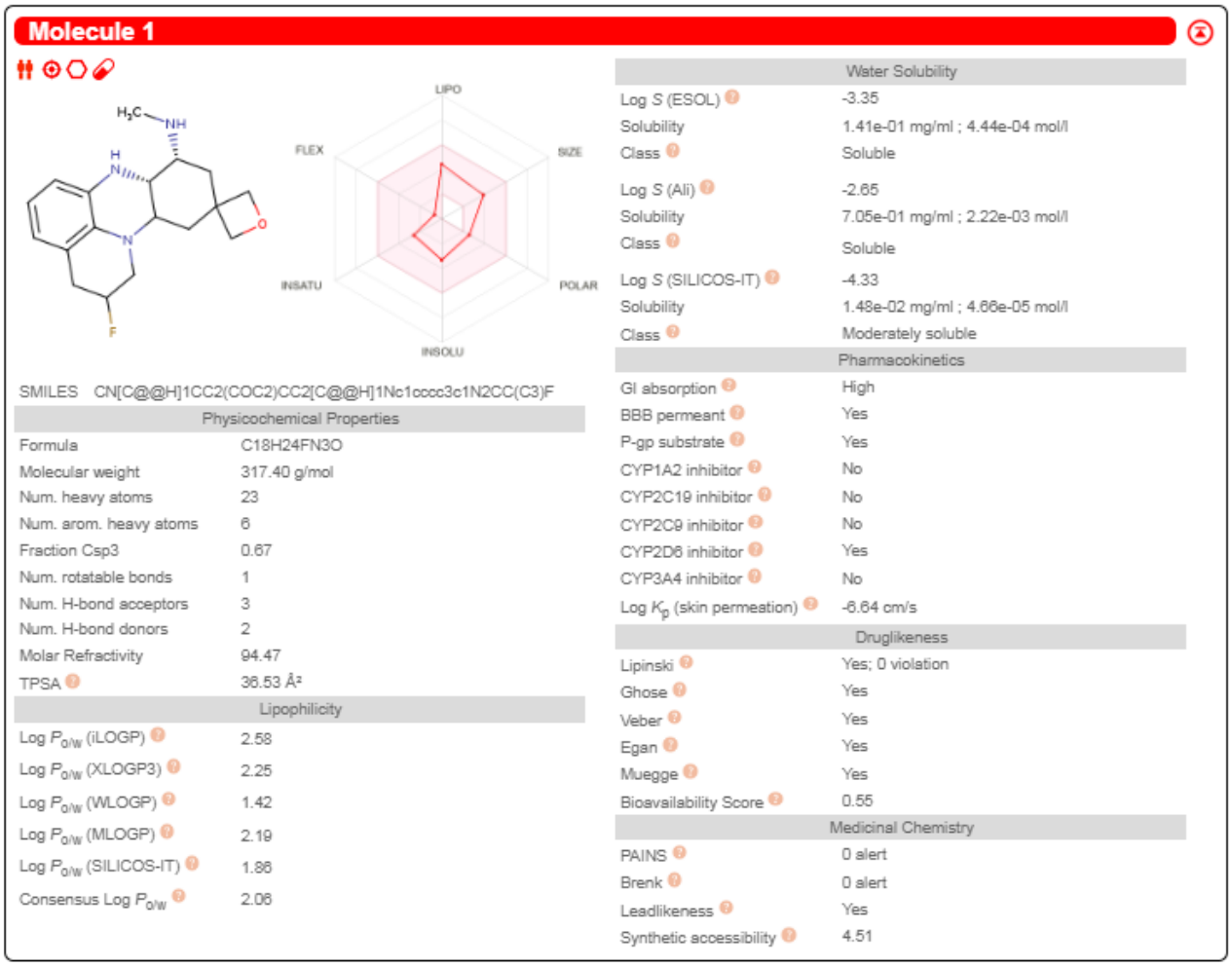

Fig. 5. ADME parameters and others of the molecule $C_{18}H_{24}FN_3O$.
Source: *http://www.swissadme.ch.*

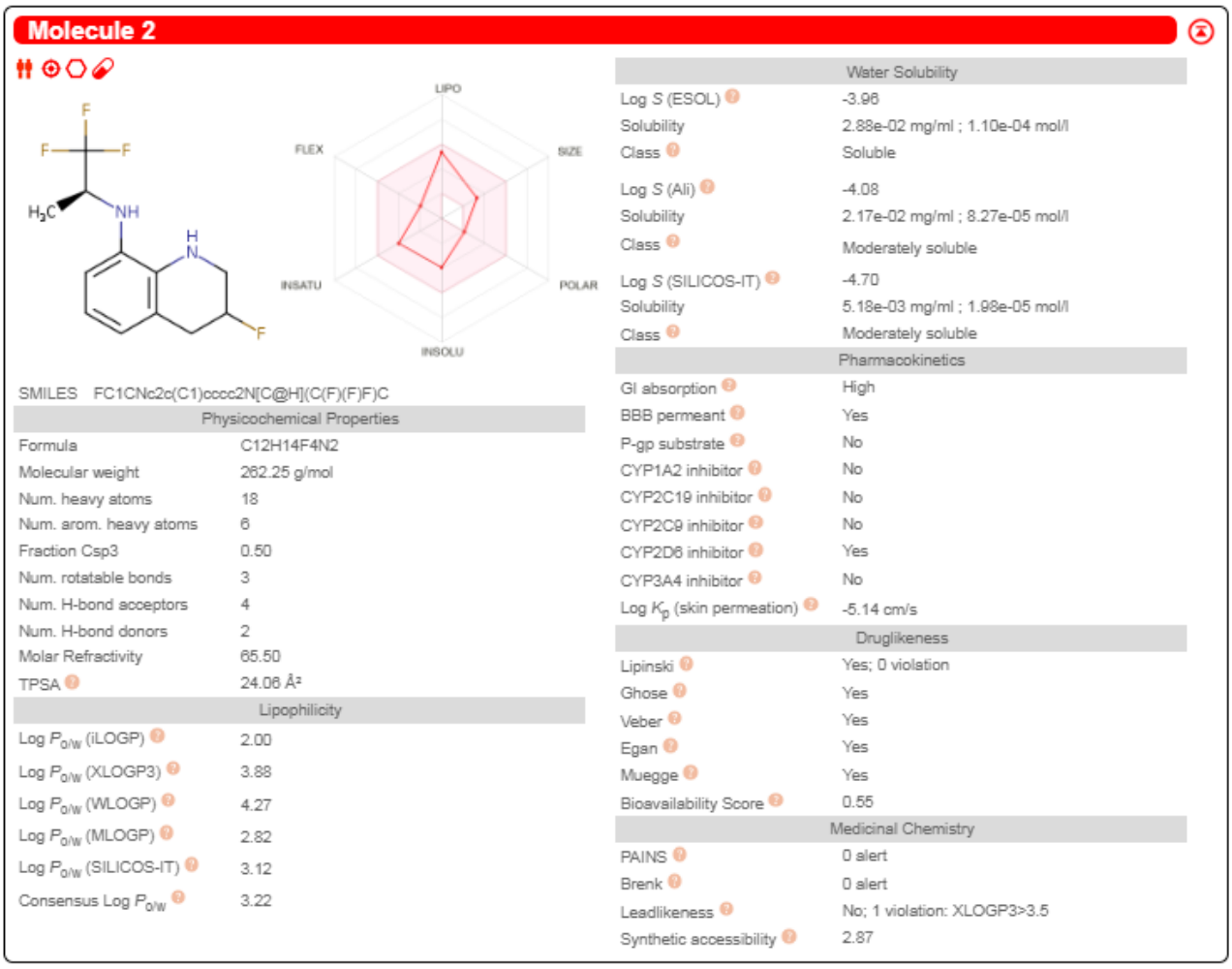

Fig. 6. ADME parameters and others of the molecule $C_{12}H_{14}F_4N_2$.
Source: *http://www.swissadme.ch.*

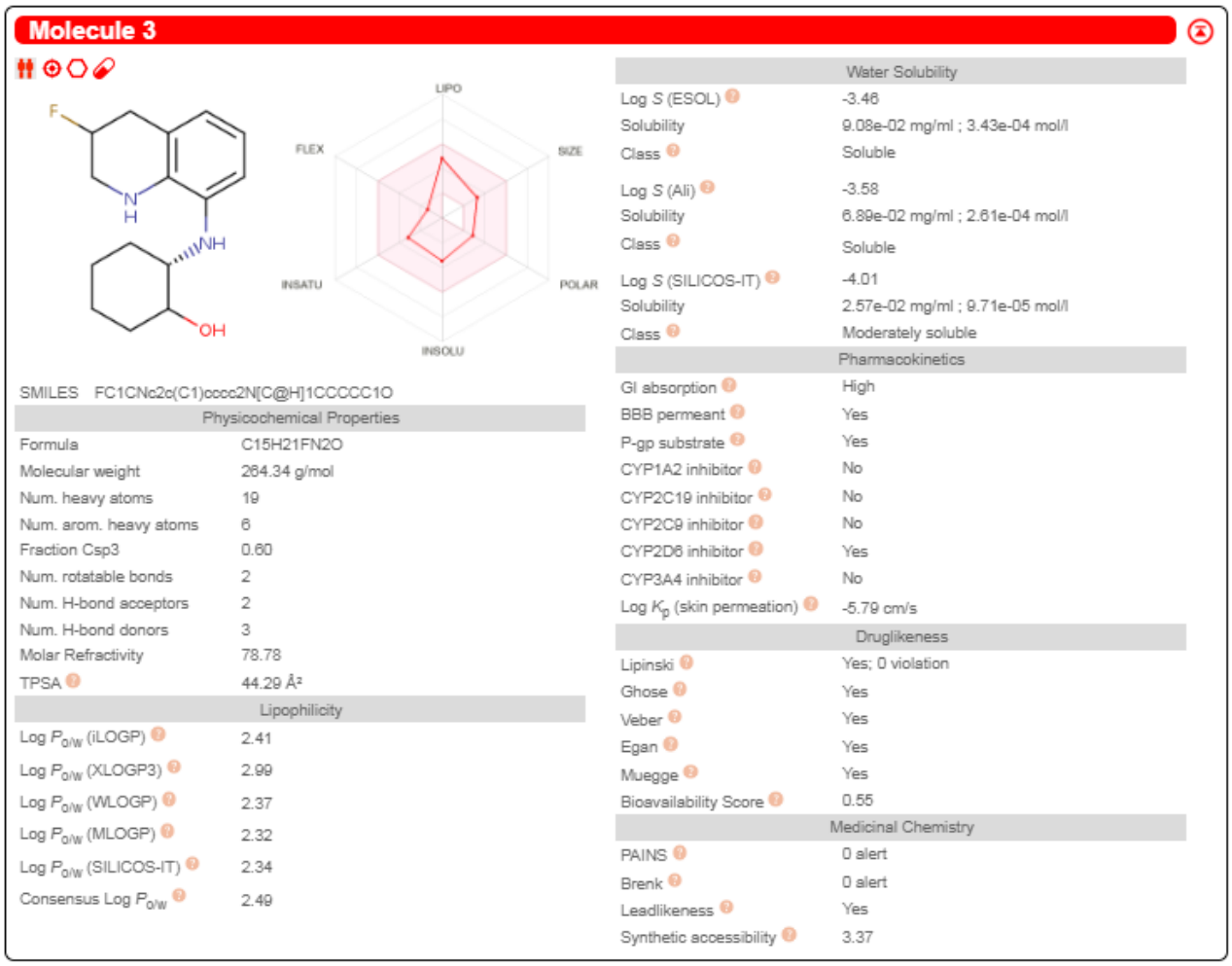

Fig. 7. ADME parameters and others of the molecule $C_{15}H_{21}FN_2O$.
Source: *http://www.swissadme.ch.*

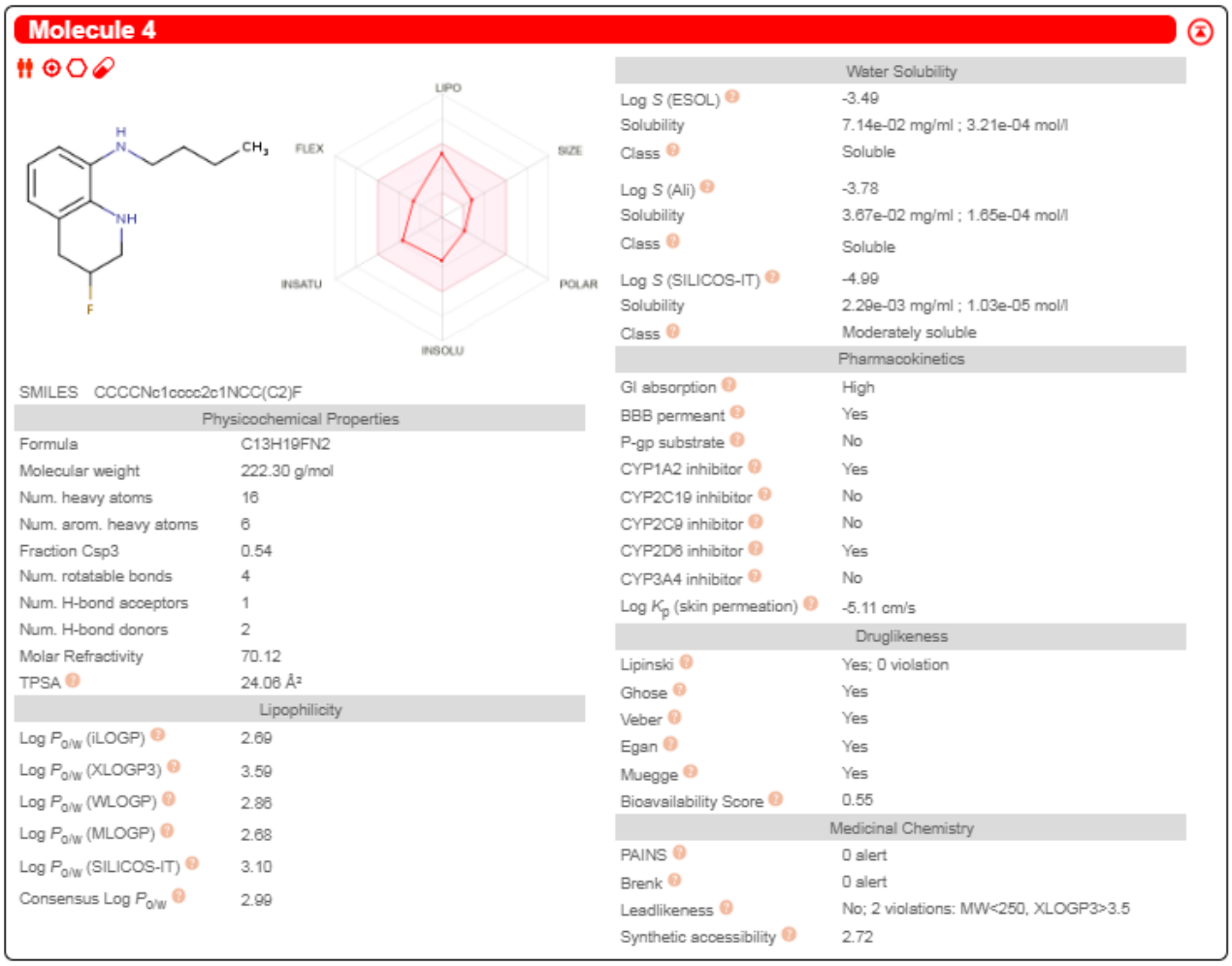

Fig. 8. ADME parameters and others of the molecule $C_{13}H_{19}FN_2$.
Source: *http://www.swissadme.ch.*

Annex 2

Target Name	ChEMBL-ID	Indication	Probability	Model accuracy
Signal transducer and activator of transcription 3	T29130	Brain cancer [ICD-11: 2A00]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Chronic lymphocytic leukaemia [ICD-11: 2A82.0]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Hepatocellular carcinoma [ICD-11: 2C12.02]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Immune System disease [ICD-11: 4A01-4B41]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Inflammation [ICD-11: 1A00-CA43.1]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Multiple myeloma [ICD-11: 2A83]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Psoriasis vulgaris [ICD-11: EA90]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Recurrent glioblastoma [ICD-11: 2A00.00]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Solid tumour/cancer [ICD-11: 2A00-2F9Z]	94.33%	82.69%
Signal transducer and activator of transcription 3	T29130	Ulcerative colitis [ICD-11: DD71]	94.33%	82.69%

Fig. 9. Indications of predicted target of the molecule $C_{18}H_{24}FN_3O$.
Source: *https://prediction.charite.de/subpages/target_prediction.php*

Target Name	ChEMBL-ID	Indication	Probability	Model accuracy
Cathepsin D	T67102	Hypertension [ICD-11: BA00-BA04]	95.13%	98.95%
Cathepsin D	T67102	Multiple sclerosis [ICD-11: 8A40]	95.13%	98.95%
Neuronal acetylcholine receptor; alpha3/beta4	T73724	Alzheimer disease [ICD-11: 8A20]	94.82%	97.23%
Neuronal acetylcholine receptor; alpha3/beta4	T73724	Tobacco dependence [ICD-11: 6C4A.2]	94.82%	97.23%
DNA-(apurinic or apyrimidinic site) lyase	T13348	Glioma [ICD-11: 2A00.0]	92.4%	91.11%
DNA-(apurinic or apyrimidinic site) lyase	T13348	Melanoma [ICD-11: 2C30]	92.4%	91.11%
DNA-(apurinic or apyrimidinic site) lyase	T13348	Ocular cancer [ICD-11: 2D00-2D07]	92.4%	91.11%
DNA-(apurinic or apyrimidinic site) lyase	T13348	Solid tumour/cancer [ICD-11: 2A00-2F9Z]	92.4%	91.11%
G-protein coupled receptor 55	T87670	Attention deficit hyperactivity disorder [ICD-11: 6A05.Z]	90.62%	78.15%
PI3-kinase p110-beta subunit	T05031	Breast cancer [ICD-11: 2C60-2C65]	90.06%	98.75%

Fig. 10. Indications of predicted target of the molecule $C_{12}H_{14}F_4N_2$.
Source: *https://prediction.charite.de/subpages/target_prediction.php*

Target Name	ChEMBL-ID	Indication	Probability	Model accuracy
DNA-(apurinic or apyrimidinic site) lyase	T13348	Glioma [ICD-11: 2A00.0]	96.22%	91.11%
DNA-(apurinic or apyrimidinic site) lyase	T13348	Melanoma [ICD-11: 2C30]	96.22%	91.11%
DNA-(apurinic or apyrimidinic site) lyase	T13348	Ocular cancer [ICD-11: 2D00-2D07]	96.22%	91.11%
DNA-(apurinic or apyrimidinic site) lyase	T13348	Solid tumour/cancer [ICD-11: 2A00-2F9Z]	96.22%	91.11%
Adenosine A1 receptor	T92072	Acute and chronic heart failure [ICD-11: BD1Z]	96.11%	95.93%
Adenosine A1 receptor	T92072	Allergy [ICD-11: 4A80-4A85]	96.11%	95.93%
Adenosine A1 receptor	T92072	Atrial fibrillation [ICD-11: BC81.3]	96.11%	95.93%
Adenosine A1 receptor	T92072	Autoimmune diabetes [ICD-11: 5A10]	96.11%	95.93%
Adenosine A1 receptor	T92072	Cardiac arrhythmias [ICD-11: BC9Z]	96.11%	95.93%
Adenosine A1 receptor	T92072	Cardiac disease [ICD-11: BA00-BE2Z]	96.11%	95.93%

Fig. 11. Indications of predicted target of the molecule $C_{15}H_{21}FN_2O$.
Source: *https://prediction.charite.de/subpages/target_prediction.php*

Target Name	ChEMBL-ID	Indication	Probability	Model accuracy
Cathepsin D	T67102	Hypertension [ICD-11: BA00-BA04]	98.71%	98.95%
Cathepsin D	T67102	Multiple sclerosis [ICD-11: 8A40]	98.71%	98.95%
HERG	T20251	Angina pectoris [ICD-11: BA40]	93.42%	89.76%
HERG	T20251	Cardiac arrhythmias [ICD-11: BC9Z]	93.42%	89.76%
HERG	T20251	Cardiac failure [ICD-11: BD10-BD13]	93.42%	89.76%
HERG	T20251	Heart arrhythmia [ICD-11: BC65]	93.42%	89.76%
HERG	T20251	Malaria [ICD-11: 1F40-1F45]	93.42%	89.76%
HERG	T20251	Multiple sclerosis [ICD-11: 8A40]	93.42%	89.76%
HERG	T20251	Ovarian cancer [ICD-11: 2C73]	93.42%	89.76%
HERG	T20251	Pain [ICD-11: MG30-MG3Z]	93.42%	89.76%

Fig. 12. Indications of predicted target of the molecule $C_{13}H_{19}FN_2$.
Source: *https://prediction.charite.de/subpages/target_prediction.php*