

## Supporting Informations

### **Synthesis, Anti-breast Cancer Assessment, and Molecular Docking Study of some New Thiazole Clubbed Thiophene Scaffolds**

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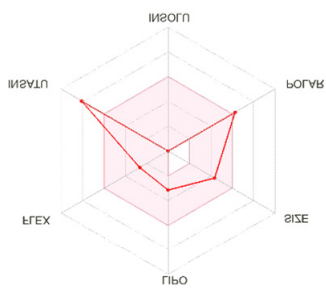
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**4a**

#### **Physicochemical Properties**

Formula	C16H16N6S2
Molecular weight	356.47 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	16
Fraction Csp3	0.12
Num. rotatable bonds	4
Num. H-bond acceptors	4
Num. H-bond donors	1

Molar Refractivity	100.32
TPSA 	136.87 Å <sup>2</sup>
Lipophilicity	
Log <i>P</i> <sub>o/w</sub> (iLOGP) 	
Log <i>P</i> <sub>o/w</sub> (XLOGP3) 	
Log <i>P</i> <sub>o/w</sub> (WLOGP) 	4.38
Log <i>P</i> <sub>o/w</sub> (MLOGP) 	
Log <i>P</i> <sub>o/w</sub> (SILICOS-IT) 	
Consensus Log <i>P</i> <sub>o/w</sub> 	
Water Solubility	
Log <i>S</i> (ESOL) 	
Solubility	mg/ml ; mol/l
Class 	
Log <i>S</i> (Ali) 	
Solubility	mg/ml ; mol/l
Class 	
Log <i>S</i> (SILICOS-IT) 	
Solubility	mg/ml ; mol/l
Class 	
Pharmacokinetics	
GI absorption 	
BBB permeant 	
P-gp substrate 	
CYP1A2 inhibitor 	
CYP2C19 inhibitor 	
CYP2C9 inhibitor 	
CYP2D6 inhibitor 	
CYP3A4 inhibitor 	
Log <i>K</i> <sub>p</sub> (skin permeation) 	cm/s
Druglikeness	
Lipinski 	; violation
Ghose 	
Veber 	
Egan 	
Muegge 	
Bioavailability Score 	

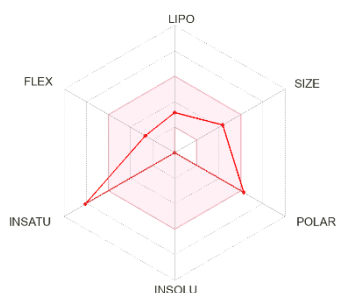
## Medicinal Chemistry

PAINS ? 0 alert

Brenk ? 0 alert

Leadlikeness ?

Synthetic accessibility ?



4b

### Physicochemical Properties

Formula C16H16N6S2

Molecular weight 356.47 g/mol

Num. heavy atoms 24

Num. arom. heavy atoms 16

Fraction Csp3 0.12

Num. rotatable bonds 4

Num. H-bond acceptors 4

Num. H-bond donors 1

Molar Refractivity 100.48

TPSA ? 136.87 Å<sup>2</sup>

### Lipophilicity

Log  $P_{o/w}$  (iLOGP) ?

Log  $P_{o/w}$  (XLOGP3) ?

Log  $P_{o/w}$  (WLOGP) ? 4.30

Log  $P_{o/w}$  (MLOGP) ?

Log  $P_{o/w}$  (SILICOS-IT) ?

Consensus Log  $P_{o/w}$  ?

### Water Solubility

Log  $S$  (ESOL) ?

Solubility mg/ml ; mol/l

Class ?

Log  $S$  (Ali) ?

Solubility mg/ml ; mol/l

Class ?

Log *S* (SILICOS-IT) ?

Solubility mg/ml ; mol/l

Class ?

### Pharmacokinetics

GI absorption ?

BBB permeant ?

P-gp substrate ?

CYP1A2 inhibitor ?

CYP2C19 inhibitor ?

CYP2C9 inhibitor ?

CYP2D6 inhibitor ?

CYP3A4 inhibitor ?

Log *K<sub>p</sub>* (skin permeation) ? cm/s

### Druglikeness

Lipinski ? ; violation

Ghose ?

Veber ?

Egan ?

Muegge ?

Bioavailability Score ?

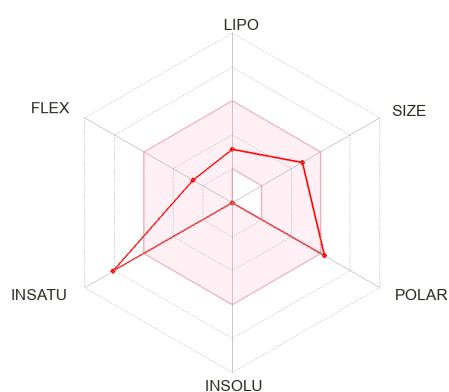
### Medicinal Chemistry

PAINS ? 0 alert


Brenk ? 0 alert

Leadlikeness ?







Synthetic accessibility ?









## Physicochemical Properties

Formula	C16H15ClN6S2
Molecular weight	390.91 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	16
Fraction Csp3	0.12
Num. rotatable bonds	4
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	105.33
TPSA 	136.87 Å²









## Lipophilicity

Log $P_{o/w}$ (iLOGP) 	
Log $P_{o/w}$ (XLOGP3) 	
Log $P_{o/w}$ (WLOGP) 	5.04
Log $P_{o/w}$ (MLOGP) 	
Log $P_{o/w}$ (SILICOS-IT) 	
Consensus Log $P_{o/w}$ 	

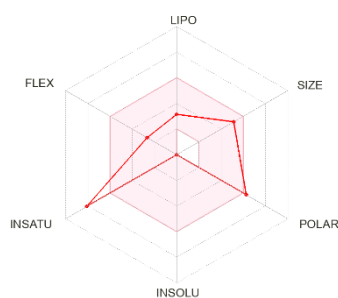
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Log $S$ (ESOL) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (Ali) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (SILICOS-IT) 	
Solubility	mg/ml ; mol/l
Class 	

## Pharmacokinetics

GI absorption 	
BBB permeant 	
P-gp substrate 	
CYP1A2 inhibitor 	
CYP2C19 inhibitor 	
CYP2C9 inhibitor 	
CYP2D6 inhibitor 	
CYP3A4 inhibitor 	

Log $K_p$ (skin permeation) ?	cm/s
Druglikeness	
Lipinski ?	; violation
Ghose ?	
Veber ?	
Egan ?	
Muegge ?	
Bioavailability Score ?	
Medicinal Chemistry	
PAINS ?	0 alert
Brenk ?	0 alert
Leadlikeness ?	
Synthetic accessibility ?	



4d

Physicochemical Properties	
Formula	C <sub>16</sub> H <sub>14</sub> Cl <sub>2</sub> N <sub>6</sub> S <sub>2</sub>
Molecular weight	425.36 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	16
Fraction Csp <sup>3</sup>	0.12
Num. rotatable bonds	4
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	110.34
TPSA ?	136.87 Å <sup>2</sup>
Lipophilicity	
Log $P_{o/w}$ (iLOGP) ?	
Log $P_{o/w}$ (XLOGP3) ?	
Log $P_{o/w}$ (WLOGP) ?	5.69
Log $P_{o/w}$ (MLOGP) ?	
Log $P_{o/w}$ (SILICOS-IT) ?	

Consensus Log  $P_{o/w}$  ?

#### Water Solubility

Log  $S$  (ESOL) ?

Solubility mg/ml ; mol/l

Class ?

Log  $S$  (Ali) ?

Solubility mg/ml ; mol/l

Class ?

Log  $S$  (SILICOS-IT) ?

Solubility mg/ml ; mol/l

Class ?

#### Pharmacokinetics

GI absorption ?

BBB permeant ?

P-gp substrate ?

CYP1A2 inhibitor ?

CYP2C19 inhibitor ?

CYP2C9 inhibitor ?

CYP2D6 inhibitor ?

CYP3A4 inhibitor ?

Log  $K_p$  (skin permeation) ? cm/s

#### Druglikeness

Lipinski ? ; violation

Ghose ?

Veber ?

Egan ?

Muegge ?

Bioavailability Score ?

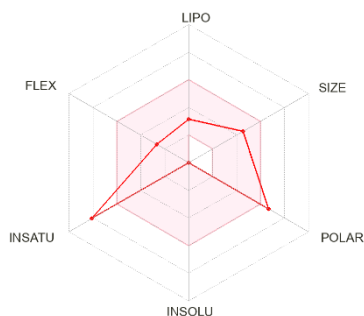
#### Medicinal Chemistry

PAINS ? 0 alert

Brenk ? 0 alert

Leadlikeness ?

Synthetic accessibility ?



8a

### Physicochemical Properties

Formula	C16H16N6OS2
Molecular weight	372.47 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	11
Fraction Csp3	0.12
Num. rotatable bonds	4
Num. H-bond acceptors	5
Num. H-bond donors	2
Molar Refractivity	108.56
TPSA	148.98 Å²

### Lipophilicity

Log $P_{o/w}$ (iLOGP)	
Log $P_{o/w}$ (XLOGP3)	
Log $P_{o/w}$ (WLOGP)	2.44
Log $P_{o/w}$ (MLOGP)	
Log $P_{o/w}$ (SILICOS-IT)	
Consensus Log $P_{o/w}$	

### Water Solubility

Log $S$ (ESOL)	
Solubility	mg/ml ; mol/l
Class	
Log $S$ (Ali)	
Solubility	mg/ml ; mol/l
Class	
Log $S$ (SILICOS-IT)	
Solubility	mg/ml ; mol/l
Class	

### Pharmacokinetics



GI absorption ?

BBB permeant ?

P-gp substrate ?

CYP1A2 inhibitor ?

CYP2C19 inhibitor ?

CYP2C9 inhibitor ?

CYP2D6 inhibitor ?

CYP3A4 inhibitor ?

Log  $K_p$  (skin permeation) ? cm/s

#### Druglikeness

Lipinski ? ; violation

Ghose ?

Veber ?

Egan ?

Muegge ?

Bioavailability Score ?

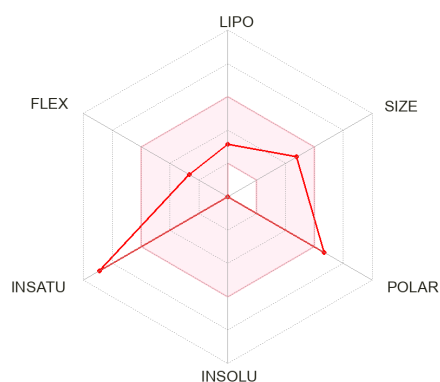
#### Medicinal Chemistry

PAINS ? 0 alert

Brenk ? 0 alert

Leadlikeness ?




























Synthetic accessibility ?



**8b**

#### Physicochemical Properties

Formula	C15H13ClN6OS2
Molecular weight	392.89 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	11
Fraction Csp3	0.07
Num. rotatable bonds	4

Num. H-bond acceptors	5
Num. H-bond donors	2
Molar Refractivity	108.60
TPSA 	148.98 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP) 	
Log $P_{o/w}$ (XLOGP3) 	
Log $P_{o/w}$ (WLOGP) 	2.78
Log $P_{o/w}$ (MLOGP) 	
Log $P_{o/w}$ (SILICOS-IT) 	
Consensus Log $P_{o/w}$ 	
Water Solubility	
Log $S$ (ESOL) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (Ali) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (SILICOS-IT) 	
Solubility	mg/ml ; mol/l
Class 	
Pharmacokinetics	
GI absorption 	
BBB permeant 	
P-gp substrate 	
CYP1A2 inhibitor 	
CYP2C19 inhibitor 	
CYP2C9 inhibitor 	
CYP2D6 inhibitor 	
CYP3A4 inhibitor 	
Log $K_p$ (skin permeation) 	cm/s
Druglikeness	
Lipinski 	; violation
Ghose 	
Veber 	
Egan 	
Muegge 	

Bioavailability Score ?

### Medicinal Chemistry

PAINS ?

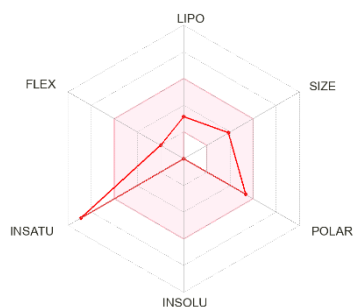
0 alert

Brenk ?

0 alert

Leadlikeness ?

Synthetic accessibility ?



**11a**

### Physicochemical Properties

Formula	C15H14N4S2
Molecular weight	314.43 g/mol
Num. heavy atoms	21
Num. arom. heavy atoms	16
Fraction Csp3	0.07
Num. rotatable bonds	3
Num. H-bond acceptors	2
Num. H-bond donors	1
Molar Refractivity	90.17
TPSA ?	112.15 Å <sup>2</sup>

### Lipophilicity

Log $P_{o/w}$ (iLOGP) ?	
Log $P_{o/w}$ (XLOGP3) ?	
Log $P_{o/w}$ (WLOGP) ?	3.32
Log $P_{o/w}$ (MLOGP) ?	
Log $P_{o/w}$ (SILICOS-IT) ?	
Consensus Log $P_{o/w}$ ?	

### Water Solubility

Log $S$ (ESOL) ?	
Solubility	mg/ml ; mol/l
Class ?	
Log $S$ (Ali) ?	

Solubility mg/ml ; mol/l

Class ?

Log *S* (SILICOS-IT) ?

Solubility mg/ml ; mol/l

Class ?

### Pharmacokinetics

GI absorption ?

BBB permeant ?

P-gp substrate ?

CYP1A2 inhibitor ?

CYP2C19 inhibitor ?

CYP2C9 inhibitor ?

CYP2D6 inhibitor ?

CYP3A4 inhibitor ?

Log *K<sub>p</sub>* (skin permeation) ? cm/s

### Druglikeness

Lipinski ? ; violation

Ghose ?

Veber ?

Egan ?

Muegge ?

Bioavailability Score ?

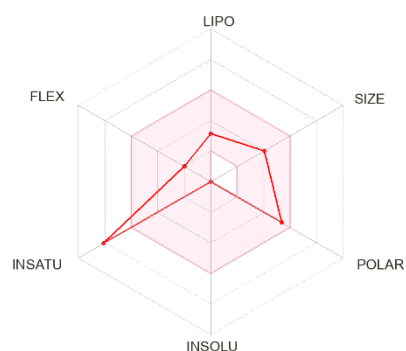
### Medicinal Chemistry

PAINS ? 0 alert

Brenk ? 0 alert























Leadlikeness ?

Synthetic accessibility



11b

Physicochemical Properties

Formula	C16H16N4S2
Molecular weight	328.46 g/mol
Num. heavy atoms	22
Num. arom. heavy atoms	16
Fraction Csp3	0.12
Num. rotatable bonds	3
Num. H-bond acceptors	2
Num. H-bond donors	1
Molar Refractivity	95.14
TPSA 	112.15 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP) 	
Log $P_{o/w}$ (XLOGP3) 	
Log $P_{o/w}$ (WLOGP) 	3.63
Log $P_{o/w}$ (MLOGP) 	
Log $P_{o/w}$ (SILICOS-IT) 	
Consensus Log $P_{o/w}$ 	
Water Solubility	
Log $S$ (ESOL) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (Ali) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (SILICOS-IT) 	
Solubility	mg/ml ; mol/l
Class 	
Pharmacokinetics	
GI absorption 	
BBB permeant 	
P-gp substrate 	
CYP1A2 inhibitor 	
CYP2C19 inhibitor 	
CYP2C9 inhibitor 	
CYP2D6 inhibitor 	
CYP3A4 inhibitor 	
Log $K_p$ (skin permeation) 	cm/s

## Druglikeness

Lipinski ? ; violation

Ghose ?

Veber ?

Egan ?

Muegge ?

Bioavailability Score ?

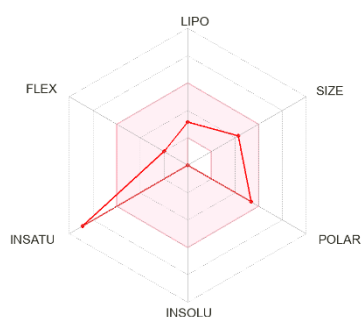
## Medicinal Chemistry

PAINS ? 0 alert

Brenk ? 0 alert

Leadlikeness ?

Synthetic accessibility ?



11c

## Physicochemical Properties

Formula C15H13ClN4S2

Molecular weight 348.87 g/mol

Num. heavy atoms 22

Num. arom. heavy atoms 16

Fraction Csp3 0.07

Num. rotatable bonds 3

Num. H-bond acceptors 2

Num. H-bond donors 1

Molar Refractivity 95.18

TPSA ? 112.15 Å<sup>2</sup>

## Lipophilicity

Log *P*<sub>o/w</sub> (iLOGP) ?

Log *P*<sub>o/w</sub> (XLOGP3) ?

Log *P*<sub>o/w</sub> (WLOGP) ? 3.98

Log *P*<sub>o/w</sub> (MLOGP) ?

Log *P*<sub>o/w</sub> (SILICOS-IT) ?

Consensus Log *P*<sub>o/w</sub> ?

## Water Solubility

Log  $S$  (ESOL) ?

Solubility mg/ml ; mol/l

Class ?

Log  $S$  (Ali) ?

Solubility mg/ml ; mol/l

Class ?

Log  $S$  (SILICOS-IT) ?

Solubility mg/ml ; mol/l

Class ?

## Pharmacokinetics

GI absorption ?

BBB permeant ?

P-gp substrate ?

CYP1A2 inhibitor ?

CYP2C19 inhibitor ?

CYP2C9 inhibitor ?

CYP2D6 inhibitor ?

CYP3A4 inhibitor ?

Log  $K_p$  (skin permeation) ? cm/s

## Druglikeness

Lipinski ? ; violation

Ghose ?

Veber ?

Egan ?

Muegge ?

Bioavailability Score ?

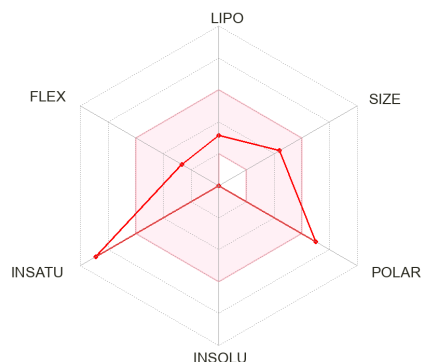
## Medicinal Chemistry

PAINS ? 0 alert

Brenk ? 0 alert

Leadlikeness ?

Synthetic accessibility



**11d**

### physicochemical Properties

Formula	C15H13N5O2S2
Molecular weight	359.43 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	16
Fraction Csp3	0.07
Num. rotatable bonds	4
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	98.99
TPSA	157.97 Å²

### Lipophilicity

Log $P_{o/w}$ (iLOGP)	
Log $P_{o/w}$ (XLOGP3)	
Log $P_{o/w}$ (WLOGP)	3.23
Log $P_{o/w}$ (MLOGP)	
Log $P_{o/w}$ (SILICOS-IT)	
Consensus Log $P_{o/w}$	

### Water Solubility

Log $S$ (ESOL)	
Solubility	mg/ml ; mol/l
Class	
Log $S$ (Ali)	
Solubility	mg/ml ; mol/l
Class	
Log $S$ (SILICOS-IT)	
Solubility	mg/ml ; mol/l
Class	

### Pharmacokinetics



GI absorption ?

BBB permeant ?

P-gp substrate ?

CYP1A2 inhibitor ?

CYP2C19 inhibitor ?

CYP2C9 inhibitor ?

CYP2D6 inhibitor ?

CYP3A4 inhibitor ?

Log  $K_p$  (skin permeation) ? cm/s

#### Druglikeness

Lipinski ? ; violation

Ghose ?

Veber ?

Egan ?

Muegge ?

Bioavailability Score ?

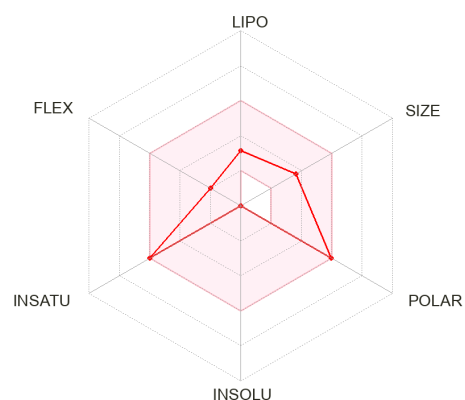
#### Medicinal Chemistry

PAINS ? 0 alert

Brenk ? 0 alert

Leadlikeness ?

Synthetic accessibility



14a

#### Physicochemical Properties

Formula C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>OS<sub>2</sub>




























Molecular weight 294.40 g/mol

Num. heavy atoms 19

Num. arom. heavy atoms 10

Fraction Csp<sup>3</sup> 0.25

Num. rotatable bonds 3

Num. H-bond acceptors	3
Num. H-bond donors	1
Molar Refractivity	79.89
TPSA 	129.22 Å <sup>2</sup>
Lipophilicity	
Log $P_{o/w}$ (iLOGP) 	
Log $P_{o/w}$ (XLOGP3) 	
Log $P_{o/w}$ (WLOGP) 	2.17
Log $P_{o/w}$ (MLOGP) 	
Log $P_{o/w}$ (SILICOS-IT) 	
Consensus Log $P_{o/w}$ 	
Water Solubility	
Log $S$ (ESOL) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (Ali) 	
Solubility	mg/ml ; mol/l
Class 	
Log $S$ (SILICOS-IT) 	
Solubility	mg/ml ; mol/l
Class 	
Pharmacokinetics	
GI absorption 	
BBB permeant 	
P-gp substrate 	
CYP1A2 inhibitor 	
CYP2C19 inhibitor 	
CYP2C9 inhibitor 	
CYP2D6 inhibitor 	
CYP3A4 inhibitor 	
Log $K_p$ (skin permeation) 	cm/s
Druglikeness	
Lipinski 	; violation
Ghose 	
Veber 	
Egan 	
Muegge 	

Bioavailability Score ?

#### Medicinal Chemistry

PAINS ?

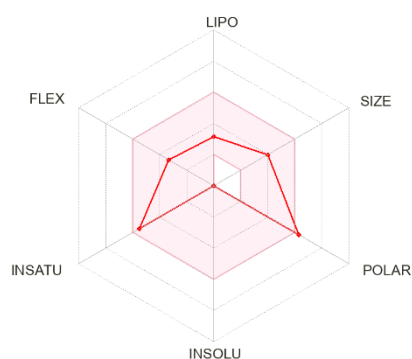
0 alert

Brenk ?

0 alert

Leadlikeness ?

Synthetic accessibility ?



14b

#### Physicochemical Properties

Formula	C13H16N4O2S2
Molecular weight	324.42 g/mol
Num. heavy atoms	21
Num. arom. heavy atoms	10
Fraction Csp3	0.31
Num. rotatable bonds	5
Num. H-bond acceptors	4
Num. H-bond donors	1
Molar Refractivity	85.79
TPSA ?	138.45 Å²

#### Lipophilicity

Log  $P_{o/w}$  (iLOGP) ?

Log  $P_{o/w}$  (XLOGP3) ?

Log  $P_{o/w}$  (WLOGP) ? 2.14

Log  $P_{o/w}$  (MLOGP) ?

Log  $P_{o/w}$  (SILICOS-IT) ?

Consensus Log  $P_{o/w}$  ?

#### Water Solubility

Log  $S$  (ESOL) ?

Solubility mg/ml ; mol/l

Class ?

Log $S$ (Ali) ?	
Solubility	mg/ml ; mol/l
Class ?	
Log $S$ (SILICOS-IT) ?	
Solubility	mg/ml ; mol/l
Class ?	
Pharmacokinetics	
GI absorption ?	
BBB permeant ?	
P-gp substrate ?	
CYP1A2 inhibitor ?	
CYP2C19 inhibitor ?	
CYP2C9 inhibitor ?	
CYP2D6 inhibitor ?	
CYP3A4 inhibitor ?	
Log $K_p$ (skin permeation) ?	cm/s
Druglikeness	
Lipinski ?	; violation
Ghose ?	
Veber ?	
Egan ?	
Muegge ?	
Bioavailability Score ?	
Medicinal Chemistry	
PAINS ?	0 alert
Brenk ?	0 alert
Leadlikeness ?	
Synthetic accessibility ?	

**Figure S1:** Extra ADME results