Supplementary file 1

Unlocking the potential of lumateperone and novel anti-psychotics for schizophrenia

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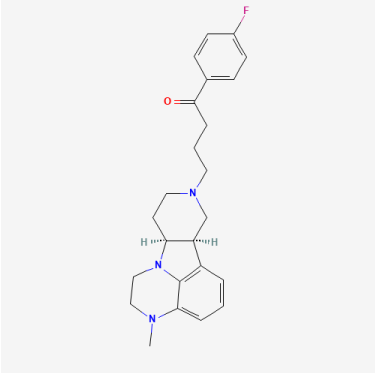

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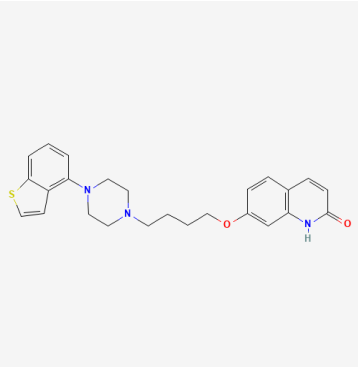

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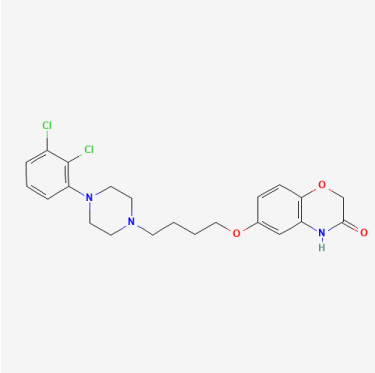

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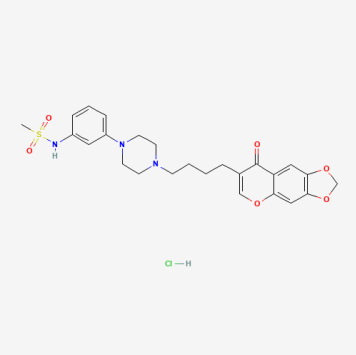

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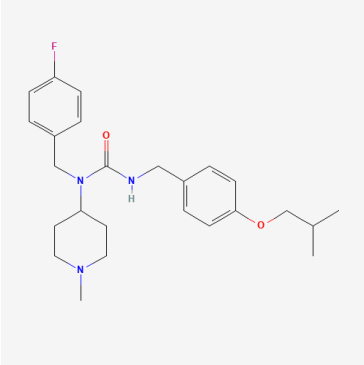

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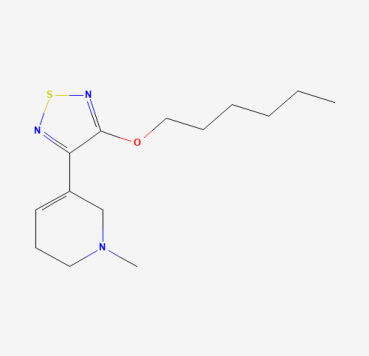

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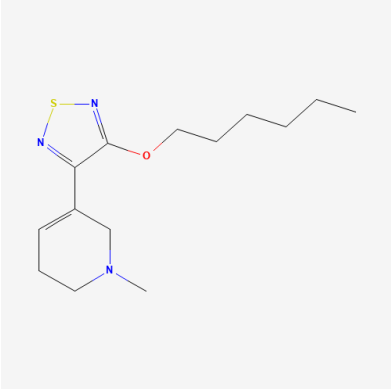

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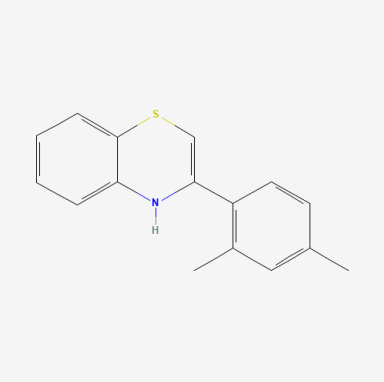

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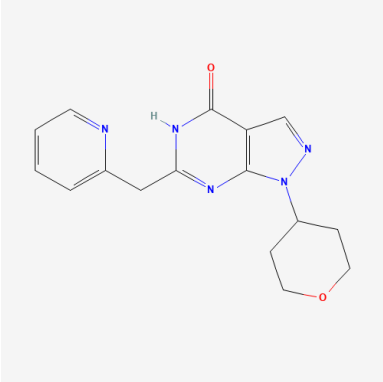

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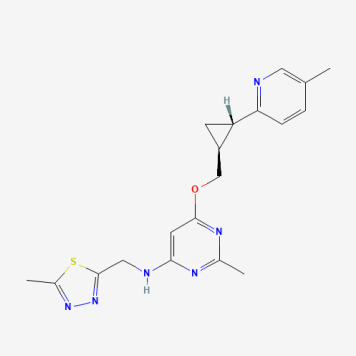

(IK)

Figure S1 - 2D structure from PUBCHEM of all mentioned drugs in this paper where (1A = Lumateperone), (1B=Brexpiprazole), (1C= Brilaroxazine), (1D= F17464), (1E=Pimavanserin), (1F=Roluperidone) , (1G= Xanomeline), (1H=BI 409306), (1I=BI 425809) (1J=MK-8189)

Table S1- Comprehensive Table on Different Anti-psychotic Drugs under clinical trials

Drug name	Mechanism of action	Dosage forms	Dosage regimens	Efficacy and clinical trials results	Unique characteristics	Side effects	Current scenario	References

Lumateperone	Agonist at presynaptic D2 receptors and an antagonist at postsynaptic D2 receptors	Oral (Tablet)	10.5 mg, 21 mg, and 42 mg, with the typical daily dose being 42 mg	In Phase I Lumateperone did not show any adverse effect as well in phase I1 and in phase II patient symptoms decreased and patient get stable with 60 mg under III and phase II trial	Show promising responses towards dopaminergic, serotonergic, and glutamatergic neurotransmission for the relief of symptoms of diiferent neuropsychiatric disorders	Constipation, sedation, fatigue, and somnolence are common side effects and hyperglycemia, orthostatic hypotension, leukopenia, neutropenia, malignant syndrome, tardive dyskinesia, EPS, and dyslipidemia are serious side effects	Trials are going on related to safety and long-term efficacy	5,23,24
Brexpiprazole	Agonist D2 receptors	Oral (Tablet)	Under trial so dosage is not finalized yet	2-4 mg of Brexpiprazole is more effective in combination and reduce severe symptoms	Brexpiprazole exhibits lower intrinsic activity as an agonist than aripiprazole.	Sleeplessness, weight gain, hypertension, and anxiety are prevalent side effects	Currently clinical trials are going on teenagers and its prevalent side effects	48,55,56
Brilaroxazine	High-affinity partial agonis	Oral (Tablet)	Under trial so dosage is not finalized	15 mg and 50 mg of Brilaroxazine show positive	It also acts on D2, D3, and D4 receptors with	EPS and akathisiaare common side	Phase II trial is complete and	59

	t on serotonin 5-HT1A and 5-HT2A receptors		yet	result in Phase II	similar chemical structure like aripiprazole	effects and increased liver enzymes is severe side effects	phase III has not started yet	
F17464	Agonist of 5-HT1A receptors while acting as a D3 antagonist	Not Clear, mostly oral (tablet)	Under trial so dosage is not finalized yet	20 mg BD of F17464 show positive result in Phase II	Remain detectable at D3 receptors for up to 22 h post-treatment, supporting its suitability for twice-daily dosing	Sleeplessness, agitation, hyperlipidemia, and akathisia are side effect reported	Cognitive ability assessment of F17464 is going on	62,65
Pimavanserin (ACP-103)	Inverse agonist at the 5HT2A receptor with high affinity and lower affinity for dopamine receptors	Not Clear	Under trial so dosage is not finalized yet	Pimavanserin reverse psychosis like behaviour without exacerbating motor difficulties in Parkinson's Disease and in phase II and III trial does not improve PANSS score	Used for treating psychosis in Parkinson's disease (PD)	Pimavanserin show side effects nausea, peripheral edema, confusion, hallucinations, constipation, and gait disturbance	Multiple trials are going on to assess tolerability and effectiveness of pimavanserin	67,68,77,78
Roluperidone	5-HT2A inhibitor and a sigma two receptor antago	Not Clear, mostly oral (tablet)	During trial 32 mg and 64 mg of roluperidone was used	Roluperidone reduce schizophrenia symptoms in Phase II and III trials but during phase III trial dosage is bit high	Act as an alpha1-adrenergic antagonist little affinity for muscarinic, cholinergic, and histaminer	During phase II trial serious side effects like vomiting, abdominal pain,	Trials are going on related to safety and long-term	79,80,85

	nist				**gic receptors**	**syncope and bradycardia**	**efficacy**	
Xanomeline	**Muscarinic activator primarily affecting M1 and M4 receptor subtypes**	**Not Clear, mostly oral**	**Under trial so dosage is not finalized yet**	**Xanomeline in combination with trospium decreases PANSS overall scores**	**Exhibit functional dopamine antagonism**	**Xanomeline show adverse effects like nausea, puking, pain in the gastrointestinal tract, salivation, diarrhoea, and constipated and Xanomeline in combination with trospium show seious adverse effect which is not disclosed**	**Xanomeline and in combination with trospium show is going on to overcome advers e effects**	**86,87**
BI 409306	**PDE9A inhibitory agent**	**Not Clear**	**Under trial so dosage is not finalized yet**	**BI 409306 did not improve MATRICS Consensus Cognitive Battery (MCCB)**	**PDE9A inhibition boost intracellular cGMP availability and NMDA receptor signalling, improving synaptic plasticity and memory function in Alzheimer's Disease**	**Eye abnormalities like blurred vision, photophobia, visual brightness, flashes, and colour disruption are observed in Phase II trial**	**Trials halted during pandemic and till date no trial or investigation started**	**90,93**

					(AD)			
BI 425809	Prevent Glycine transporter 1 (GlyT1), and improving glutamate's effect on NMDA receptors	Not Clear, mostly oral	During trial 10 mg and 25 mg is used but need to be finalized	BI 425809 does not show any positive result in phase II and III trials	Focus on cognition and memory in disorders like AD and half-life of more than 30 hour	Side effects like headaches, drowsiness, and problems with the digestive tract with reduced hemoglobin level noticed but no EPS	No further update as till phase III no promising result	93,94,95
MK-8189	Phosphodiesterase 10A inhibitor modifies the dopamine D1-direct and D2-indirect striatal pathways and controls striatal glutamate receptor phosphoryla	Not Clear, mostly oral (tablet)	During phase II trial 16 and 24 mg dosages but need to be finalized	MK-8189 did not show any promising result	Half-life of 7.6 to 10.9 hr	Final findings of NCT03565068 on MK-8189 has not been released	Extensive phase II trial is being conducted to evaluate MK-8189 at 16 and 24 mg dosages	103,104,108

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