Enveric Biosciences Inc.
245 First Street, Riverview II, 18th Floor
Cambridge, MA 02142
www.Enveric.com

Enveric Biosciences Inc - Chemical Library Catalogue Brochure:
Melatonin Receptor Agonist (MRA) Compound Series

Enveric's MRA Series:
These sixteen Melatonin Receptor binding compounds are anticipated to be agonists of the melatonin receptors MT1 and MT2. Within this library are compounds with expanded receptor binding profiles.

Background:
Melatonin, a natural indolamine, is essential for regulating circadian rhythm in mammals (a.k.a. sleep-wake cycles). Melatonin is often used in to treat various sleep disorders.
The naphthalene-based compound, Agomelatine (sold by others as Valdoxan™ or Thymanax™), is an atypical antidepressant commonly used to treat Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD) in Europe and Australia. Agomelatine is a Melatonin Receptor (MT1) agonist, and also acts as an antagonist of the 5-HT2B and 5-HT2C receptors.

Key Features of the MRA Series:
- All compounds have strong binding to MT1
- MRA-01 to -08 show selective MT1 binding
- MRA-09 to MRA-16 demonstrate expanded receptor binding profiles:
  - Compounds MRA-09 to -16 bind 5-HT2B, 5-HT2C, or both receptors; these receptors are targets antagonized by Agomelatine
  - MRA-14 and MRA-16 bind SERT and 5-HT1A, which are receptors targeted by the antidepressant Vortioxetine
  - MA16 binds 5-HT2A; literature indicates that binding to 5-HT2A induces hallucinations in humans and also induces neuroplasticity
  - MRA-16 binds 5-HT1C; literature identifies various antidepressants that bind this receptor (eg. imipramine, trazodone), and suggest this interaction is important for antidepressant activity of these drugs

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Summary of *in vitro* Binding Data:

	Specific Target Receptor Binding						
Compound ID	MT1	SERT	5-HT1A	5-HT1C	5-HT2A	5-HT2B	5-HT2C
MRA-01	✓✓✓						
MRA-02	✓✓✓						
MRA-03	✓✓✓						
MRA-04	✓✓✓						
MRA-05	✓✓✓						
MRA-06	✓✓✓						
MRA-07	✓✓						
MRA-08	✓✓						
MRA-09	✓✓✓					✓✓	✓
MRA-10	✓✓✓					✓✓	✓✓
MRA-11	✓✓✓						✓✓
MRA-12	✓✓					✓✓	
MRA-13	✓✓					✓✓	
MRA-14	✓✓✓	✓	✓✓				✓
MRA-15	✓✓✓						✓✓
MRA-16	✓✓	✓✓✓	✓✓	✓✓	✓✓✓	✓✓✓	✓✓✓