ACS Chemical Neuroscience

Editorial

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ACS Chemical Neuroscience and Neuroscience Drug Discovery as 2012 Comes to a Close

Well, 2012 is almost over—hard to believe. *ACS Chemical Neuroscience* has now been publishing high quality neuroscience research for three years! The year 2012 presented several major milestones for *ACS Chemical Neuroscience*: we received our first impact factor (3.676) based on 2011 metrics, and we expanded our Associate Editors to include Dr. Anne Andrews (UCLA). In addition, both the number of manuscripts submitted to *ACS Chemical Neuroscience* and the number of citations to *ACS Chemical Neuroscience* manuscripts (Web of Science) has dramatically increased in 2012. In 2012, we also had our first thematic crossover issue with the *Journal of Medicinal Chemistry* and *ACS Medicinal Chemistry Letters* on Alzheimer's disease (AD).[1] From myself, the Associate Editors, and all at ACS, we want to extend a heartfelt thank you to all of the contributing authors to *ACS Chemical Neuroscience* since our launch in 2010, and for making *ACS Chemical Neuroscience* a desirable venue to publish your best neuroscience research.

As for neuroscience drug discovery, 2012 witnessed a number of low points, with multiple companies pulling out of neuroscience drug discovery and a long list of phase II failures of CNS therapeutics (both small molecules and biologics), and in particular for AD[1] and schizophrenia. Of these, the disappointing news that the Lilly $mGlu_{2/3}$ agonist, Pomaglumetamed Methionil, was unlikely to be positive in its primary end points in a phase III schizophrenia trial, that led the company to halt development.[2] This is especially sad news, as the positive phase II data energized the industry with success of a nondopaminergic, novel mechanism for schizophrenic patients.

However, as 2012 draws to a close, two bright lights have appeared. Janssen Pharmaceuticals and Addex Therapeutics announced that ADX71149, an $mGlu_2$ positive allosteric modulator (PAM), demonstrated safety and tolerability as well as top-line data from a phase IIa monotherapy study in schizophrenic patients.[3] A phase IIb trial is underway to explore the potential of the $mGlu_2$ PAM as an adjunctive therapy with standard antipsychotics. Will the PAM succeed where the agonist failed? Speculation on neuroscience blogs suggests the agonist, with chronic dosing, may have desensitized the receptor. It will be most interesting to follow ADX71149 as it progresses through development to test the PAM mechanism, the target ($mGlu_2$) and to offer a new therapeutic alternative to schizophrenic patients.

Addex Therapeutics' Dipraglurant, an $mGlu_5$ negative allosteric modulator (NAM), was just named one of the "Top 10 Neuroscience Projects" to watch by Windhover and Virginia Herndon. Dipraglurant is an oral $mGlu_5$ NAM that has demonstrated both safety and tolerability as well as efficacy in Parkinsons patients with leva-DOPA-induced diskinesias (LID).[3] Efficacy was observed at both 50 and 100 mg doses. Moreover, Dipraglurant reduced dystonia severity and chorea, the two major components of LID. Overall, this is very exciting data for the approach of allosteric modulation of GPCRs and for patients suffering from LID; phase III data is eagerly awaited.

In 2013, we plan to continue Viewpoint features on CNS therapeutics and solicit ideas and Viewpoints from the community. Again, we want *ACS Chemical Neuroscience* to also serve as a forum for scientific exchange on neuroscience and encourage your participation. We have a number of exciting things planned for 2013—visit the *ACS Chemical Neuroscience* Web site often for updates.

Craig W. Lindsley, Editor-in-Chief

DEDICATION

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

REFERENCES

(1) Lindsley, C. W. (2012) Alzheimer's disease: Development of Disease-Modifying Treatments is the Challenge for Our Generation. *ACS Chem. Neurosci. 3*, 804−805.

(2) Data from the Eli Lilly & Co. See www.lilly.com.

(3) Data from Addex. See www.addextherapetuics.com.

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