

June 6, 2012

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**Attention: Katri Wegelius**

**By FedEx: 7984-7713-8886**

Dear Kai:

In response to your emails of May 28, 2012 and June 3, 2012 and as promised in my email of June 1, 2013 are samples of the following two peptides.

**Selective AVP V<sub>1a</sub>/V<sub>2</sub> Antagonist**



CL-14-88

M.W. 1165.4 ~ 5 mg

**Please note that this material is synthetic. It is non-toxic, non-infectious and non-hazardous.**

<sup>a</sup>Original synthesis and some pharmacological properties in rat bioassays are reported in:

M. Manning, S. Stoev, K. Bankowski, A. Misicka, B. Lammek, N.C. Wo and W.H. Sawyer. Synthesis and Some Pharmacological Properties of Potent and Selective Antagonists of the Vasopressor (V<sub>1</sub>-receptor) Response to Arginine Vasopressin. *J. Med. Chem.* **35**:382-388, 1992.

<sup>b</sup>Its pharmacological properties in rat bioassays are given in Table 9 (peptide 4) on page 484 in the review entitled: **“Peptide and non-peptide agonists and antagonists for the vasopressin and oxytocin V<sub>1a</sub>, V<sub>1b</sub>, V<sub>2</sub> and OT receptors: research tools and potential therapeutic agents”**, Maurice Manning, Stoytcho Stoev, Bice Chini, Thierry Durroux, Bernard Mouillac, and Gilles Guillon in: *Advances in Vasopressin and*

Oxytocin – from Genes to Behaviour and Diseases (eds. Inga Neumann and Rainer Landgraf), *Progress in Brain Research* **170**:473-512, 2008. **(A pdf of this review is attached).**

<sup>c</sup>This V<sub>1a</sub> antagonist is slightly more potent than the more widely used d(CH<sub>2</sub>)<sub>5</sub>[Tyr(Me)<sup>2</sup>]AVP (Manning Compound) (Table 9 (peptide 1) in review). In contrast to d(CH<sub>2</sub>)<sub>5</sub>[Tyr(Me)<sub>2</sub>]AVP, which is a weak V<sub>2</sub> agonist, this peptide is a weak V<sub>2</sub> antagonist.

Its Antivasopressor pA<sub>2</sub> = 8.75

Its Antiantidiuretic pA<sub>2</sub> = ~ 6.0

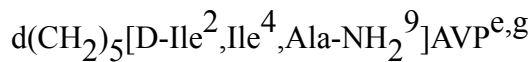
ED Ratio = ~590

Its oxytocic properties and V<sub>1b</sub> properties have not been evaluated.

<sup>d</sup>This peptide has been used in a number of published studies carried out in the laboratory of Ewa Szczepańska-Sadowska. See for example:

Cudnoch-Jedrzejewska A, Dobruch J, Puchalska L, Szczepańska-Sadowska E. Interaction of AT1 receptors and V<sub>1a</sub> receptors-mediated effects in the central cardiovascular control during the post-infarct state. Regul Pept. 2007 Aug 16; 142(3):86-94. Epub 2007 Feb. 15. Erratum in: Regul Pept. 2007 Dec 4; 144(1-3):131.

### **Potent and Selective AVP V<sub>2</sub>/V<sub>1a</sub> Antagonist**



ST-12-73

M.W. 1086.4 ~ 3.0 mg

<sup>e</sup>Its pharmacological properties in rat bioassays are reported in: W.H. Sawyer, K. Bankowski, A. Misicka, E. Nawrocka, M. Kruszynski, S. Stoev, W.A. Klis, J.P. Przybylski and M. Manning. Potent V<sub>2</sub> vasopressin antagonists with structural changes at their C-terminals. *Peptides* 9:157-163, 1988.

<sup>f</sup>See also Peptide 5, Table 7, page 613 in recent review entitled “**Oxytocin and vasopressin agonists and antagonists as research tools and potential therapeutics**”. *Journal of Neuroendocrinology* 24:609-628, 2012. (Attached here as a pdf).

As reported in these references this peptide has the following antiantidiuretic (anti-V<sub>2</sub>) and antivasopressor (anti-V<sub>1a</sub>) potencies. Its antioxytotic potencies have not been determined.

Anti V<sub>2</sub> pA<sub>2</sub> = 8.16 (ED = 0.46 nMole/Kg)

Anti V<sub>1a</sub> pA<sub>2</sub> = 6.25 (ED = 38 nmole/Kg)

It is 83 times more potent as a V<sub>2</sub> antagonist than as a V<sub>1a</sub> antagonist.

You can find citations to the use of this V<sub>2</sub> antagonist through the ISI Web of Science or Pub Med.

<sup>g</sup>With regard to the storage of these peptides, I hope the following is helpful. In the powder form, they are stable for months when stored at room temperature and for years when stored in the refrigerator. Sterile aqueous solutions are stable at room temperature for two to three weeks and for many months when stored in the refrigerator at +4 degree C.

I hope that these peptides will be useful in your studies on the role of the V<sub>1a</sub> receptor in the regulation of the BBB Na/H exchanger in postnatal rats.

Best regards,

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MM/amc

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Sent by Fedex: Wednesday, June 6, 2012

Expected Date of Delivery: Friday, June 8, 2012

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F. Lévy, Ph.D., H.D.R.

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