Product Name: AMN 082 dihydrochloride **Cat. No. 2385**

Guidelines for use

Due to the novel nature of this product, AMN082 has not yet been fully investigated. Based on data provided by the researchers who pioneered this compound (Dr. Peter J. Flor & colleagues at Novartis Pharma AG), the following guidelines are provided to optimize your use of this compound and to facilitate the interpretation of your results.

Stability Guidelines

Due to the novelty of this product, information regarding stability is limited. As a general guide for products where stability data is limited we suggest that stock solutions are prepared as aliquots in tightly sealed vials and stored at -20°C for up to one month. Before use the product should be allowed to equilibrate to room temperature for at least 60 minutes; the solution should be clear, without precipitations, and colorless. Once removed from -20°C, and brought to room temperature, it is recommended that the solution is used immediately.

Solubility Guidelines

Stock solutions (up to 10 mM) can be prepared in DMSO or methanol.

Guidelines for *in vitro* use

Non-specific actions may be observed at concentrations of 3-10 µM and above. Therefore, for researchers wishing to investigate selective mGluR7 actions, it is recommended that this product is not used above concentrations of 1 µM.

Guidelines for *in vivo* use

Guidelines for maximally tolerated doses *in vivo* are:

- 6 mg/kg p.o. in mice
- 20 mg/kg p.o. in rats

Those doses result in mGluR7-dependent physiological effects, e.g. modulation of stress-hormones. However, non-selective effects have been observed at higher doses (2-3 times higher than those stated above). Examples of such non-selective effects include head twists and tremor observed in mGluR7+/+ (wild-types) and mGluR7-/- mice (knock-outs).

The product can be orally administered (p.o.) in a methylcellulose suspension. For further details you may contact Dr. John F. Cryan at University College Cork (johnfcryan@gmail.com). There is currently no data available on maximally tolerated doses for i.v., i.c.v., or i.p. routes of administration.

Use of knock-outs (KO) for validation of data

Dr. Peter J. Flor and his colleagues recommend that the physiological and pharmacological effects of AMN082 should ideally be confirmed by evaluation in mGluR7+/+ (wild-types) versus mGluR7-/- mice (KO). Effects of

AMN082 that are seen in mGluR7+/+ (wild-types) but not in mGluR7-/- mice (KO) are most likely mGluR7-mediated.

For details on obtaining mGluR7+/+ (wild-types) and mGluR7-/- mice (KO) please contact Dr. Peter J. Flor at Novartis Pharma AG (peter_josef.flor@novartis.com) or Dr. Herman van der Putten (p_herman.van_der_putten@novartis.com).