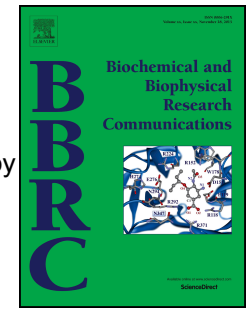
Accepted Manuscript



Pharmacological characterization of synthetic serine palmitoyltransferase inhibitors by biochemical and cellular analyses

Ryutaro Adachi, Yasutomi Asano, Kazumasa Ogawa, Motomi Oonishi, Yukiya Tanaka, Tomohiro Kawamoto

PII: S0006-291X(16)32254-9

DOI: 10.1016/j.bbrc.2016.12.182

Reference: YBBRC 37056

To appear in: *Biochemical and Biophysical Research Communications*

Received Date: 19 December 2016

Accepted Date: 28 December 2016

Please cite this article as: R. Adachi, Y. Asano, K. Ogawa, M. Oonishi, Y. Tanaka, T. Kawamoto, Pharmacological characterization of synthetic serine palmitoyltransferase inhibitors by biochemical and cellular analyses, *Biochemical and Biophysical Research Communications* (2017), doi: 10.1016/j.bbrc.2016.12.182.

Pharmacological Characterization of Synthetic Serine Palmitoyltransferase Inhibitors by Biochemical and Cellular Analyses

Ryutaro Adachi[a*], Yasutomi Asano[b], Kazumasa Ogawa[a], Motomi Oonishi[a], Yukiya Tanaka[a], and Tomohiro Kawamoto[a]

[a]Biomolecular Research Laboratories, Takeda Pharmaceutical Company Limited, 26-1, Muraoka-higashi 2-chome, Fujisawa, Kanagawa 251-8555, Japan

[b]Oncology Drug Discovery Unit, Takeda Pharmaceutical Company Limited, 26-1, Muraoka-higashi 2-chome, Fujisawa, Kanagawa 251-8555, Japan

[*]Corresponding author

E-mail: ryutaro.adachi@takeda.com (RA)

Abstract

Human serine palmitoyltransferase (SPT) is a PLP-dependent enzyme residing in the endoplasmic reticulum. It catalyzes the synthesis of 3-ketodihydrosphingosine (3-KDS) from the substrates palmitoyl-CoA and L-serine. It is a rate-limiting enzyme for sphingolipid synthesis in cells. In the present study, we characterized and pharmacologically profiled a series of tetrahydropyrazolopyridine derivatives that potently inhibit human SPT enzymatic activity, including two cell-active derivatives and one