Pyrazolo[3,4-*d*]pyrimidine active on Neuroblastoma cells

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c-Src is a tyrosine kinase belonging to the Src-family kinases (SFKs) which are a group of proteins involved in cancer development. Recently, c-Src has been reported to play an important role in the differentiation, cell-adhesion and survival of neuroblastoma (NB) cells [1]. NB is the most common extracranial pediatric solid tumor and usually undergoes rapid progression with a poor prognosis upon metastasis. Some of the pyrazolo[3,4-*d*]pyrimidine synthesized by our research group are c-Src inhibitors. In particular, compound SI306 (Figure) showed *in vivo* activity in a xenograft model using SH-SY5Y cells as well as optimal ADME characteristics [2]. With the aim of performing SAR (structure-activity relationship) studies, we synthesized a new library of SI306 analogues. Furthermore, in order to get further insights into the biological data, we tested this promising compound on the human MYCN-amplified neuroblastoma cell lines HTLA-230 and SK-N-BE-2C. In fact, amplification of MYCN, correlates with high-risk disease and poor prognosis [3]. The synthesis of the new derivatives and their biological results will be reported in the poster section.

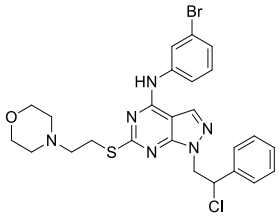

Figure: Structure of SI306

[1]Wheeler DL, Iida M, Dunn EF. *Oncologist* **2009**; 14:667-78.

[2]Tintori C1, Fallacara AL, Radi M, Zamperini C, Dreassi E, Crespan E, Maga G, Schenone S, Musumeci F, Brullo C, Richters A, Gasparrini F, Angelucci A, Festuccia C, Delle Monache S, Rauh D, Botta M., *J Med Chem*. **2015**; 58(1):347-61.

[3]Cohn SL, Pearson AD, London WB, Monclair T, Ambros PF, Brodeur GM, Faldum A, Hero B, Iehara T, Machin D, Mosseri V, Simon T, Garaventa A, Castel V, Matthay KK., *J Clin Oncol* **2009**; 27:289-97.