6-Substituted pyrazolo[3,4-*d*]pyrimidines: new promising compounds in the fight against Neuroblastoma

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Neuroblastoma (NB) is the most common extracranial pediatric solid tumor and it is responsible for the 15% of all pediatric deaths.[1] Recently, it has been shown that the tyrosine kinase c-Src plays a key role in protecting NB cells from apoptosis, thus representing an attractive target against this tumor.[2]

In this context, we reported a series of pyrazolo-pyrimidines **1** endowed with a good balance of ADME properties and activity against Src.[3] Moreover, we recently showed that compounds **2** are active against SH-SY5Y human NB cell lines at sub-micromolar concentrations.[4]

On the basis of these interesting results and of computational studies that highlighted the importance of a *meta*-hydroxy anilino group at C4, we report the synthesis of Src inhibitors **3** (***Figure 1***) as antiproliferative agents on NB cell lines.

Very interestingly, some of these derivatives confirmed the modeling predictions and resulted active on SH-SY5Y human NB cell lines at concentrations of 0.1-1 μM, maintaining good ADME properties. Thus, compounds **3** represent a promising starting point for the development of other derivatives potentially active in NB therapy.

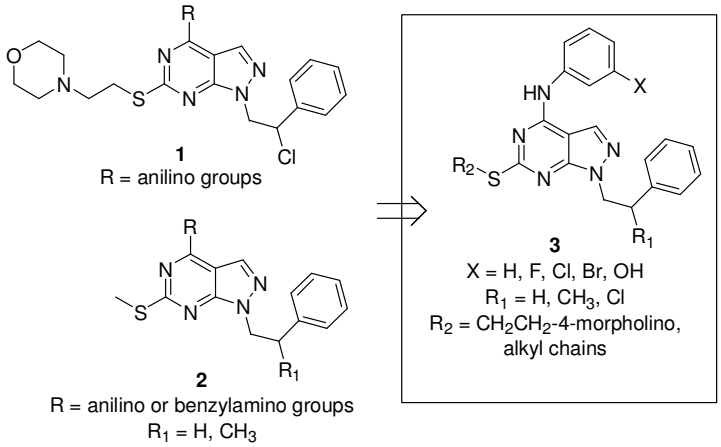

Figure 1. *General structure of compounds **3**, synthesized on the basis of previously reported compounds **1** and **2** and molecular modeling studies.*

[1] *Expert Opin. Emerging Drugs* **2013**, *18*, 155.
[2] *Oncologist* **2009**, *14*, 667.
[3] *J. Med. Chem.* **2011**, *54*, 2610.
[4] *Bioorg. Med. Chem. Lett.* **2011**, *21*, 5928.

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