

**CHEM**MED**CHEM**

Supporting Information

**Elucidation of an Allosteric Mode of Action for a Thienopyrazole ROR $\gamma$ t Inverse Agonist**

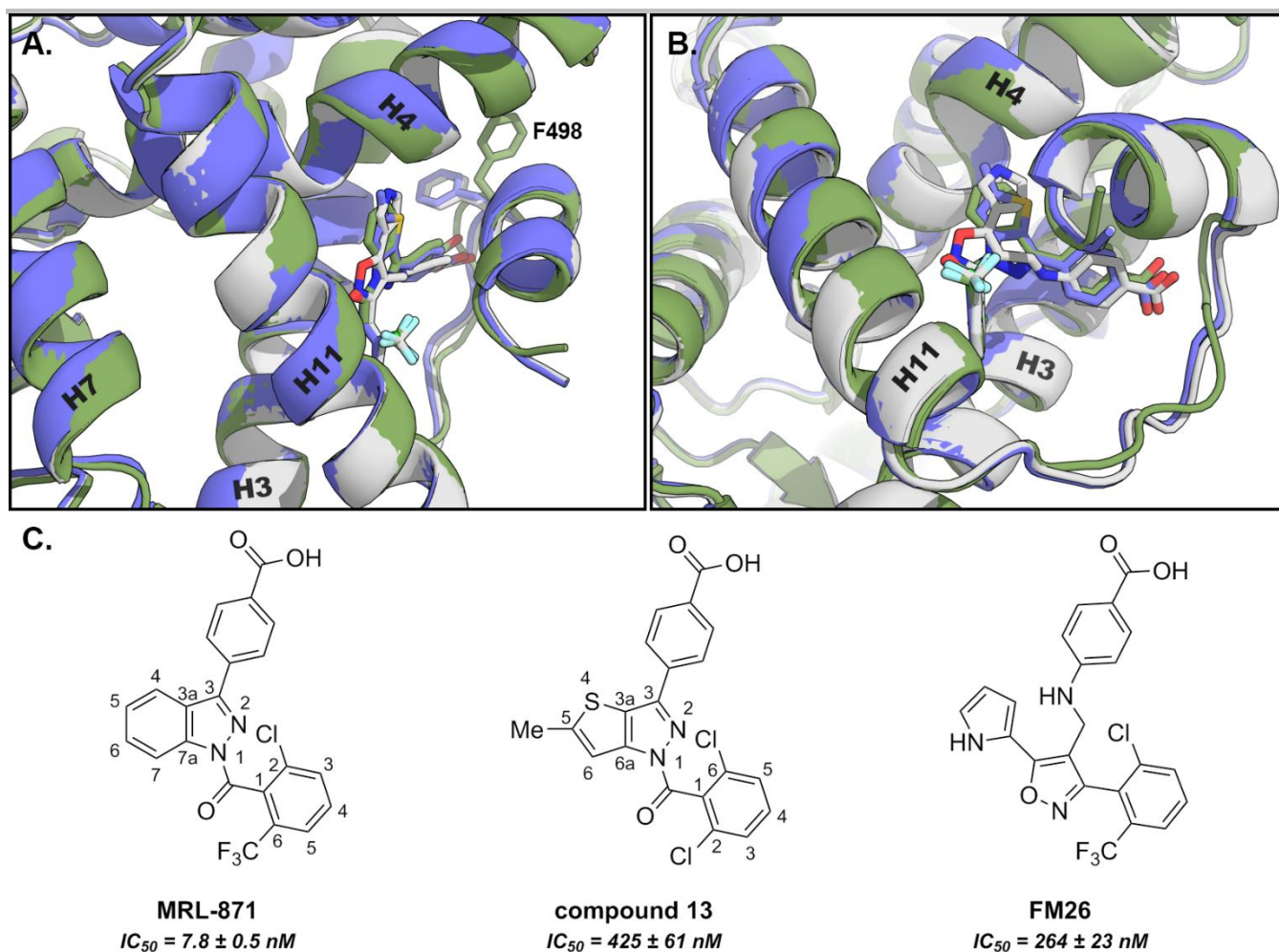
Rens M. J. M. de Vries, Richard G. Doveston, Femke A. Meijer, and Luc Brunsveld\*© 2020 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

**Table S1.** Data collection and refinement statistics for the crystal structure of ROR $\gamma$ t in complex with Glenmark's compound **13**.

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<i>ROR<math>\gamma</math>t in complex with compound 13</i>	
<i>Data collection</i>	
Space group	P 6 <sub>1</sub> 2 2
Cell dimensions	
a, b, c (Å)	107.528 107.528 98.737
$\alpha$ , $\beta$ , $\gamma$ (°)	90, 90, 120
Resolution (Å)	93.12-2.32 (2.40-2.32)
I / $\sigma$ (I)	6.9 (0.8)
Completeness (%)	100.00 (100.00)
Redundancy	35.9 (36.5)
CC <sub>1/2</sub>	0.992 (0.422)
<i>Refinement</i>	
No. unique reflections	15190 (1448)
R <sub>work</sub> /R <sub>free</sub>	0.2054/0.2520
No. atoms (non-H)	
Protein	2020
Ligand	28
Water	23
Average B-factors	
Protein	58.86
Ligand	52.19
Water	57.94
R.m.s. deviations	
Bond lengths (Å)	0.016
Bond angles (°)	2.024
<i>PDB ID</i>	6TLM

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**Figure S1.** (A-B) Crystal structure comparison of ROR $\gamma$ t in complex with **MRL-871** (green, PDB: 5C4O), **FM26** (white, PDB: 6SAL) and compound **13** (blue, PDB: 6TLM). Compound **13** and **FM26** induce the same fold of the loop between helix 11 and 12, by the interaction between the benzoic acid on the ligand and F498 of ROR $\gamma$ t. (C) Chemical structures of **MRL-871**, compound **13** and **FM26** showing the IUPAC atom numbering. The  $IC_{50}$ -values of the ligand-ROR $\gamma$ t complexes were measured previously using a TR-FRET coactivator recruitment assay.<sup>[16]</sup>