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Structure-Based Discovery of Novel Chemical Classes of Autotaxin Inhibitors

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The crystal structure of ATX in complex with a known inhibitor (HA-155) was used as a molecular model docking reference, yielding a priority list of 30 small molecule ATX inhibitors, validated by a well-established enzymatic assay of ATX activity. The two most potent, novel and structurally different compounds were further structurally optimized by deploying further in silico tools, resulting to the overall identification of six new ATX inhibitors that belong to distinct chemical classes than existing inhibitors.

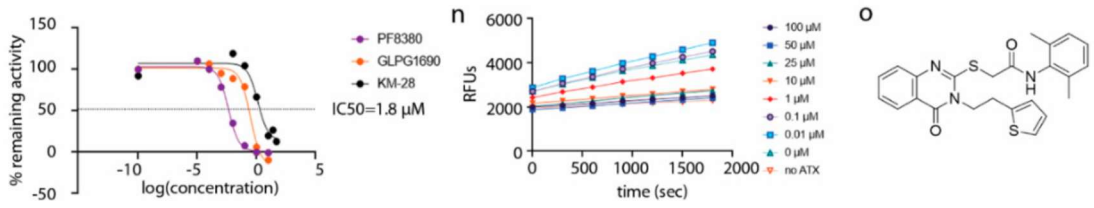

Figure. Example of a new ATX inhibitor (KM-28). PF8380 and GLPG1690 served as positive controls.