SUPPORTING INFORMATION

Code and data

The code used in this study is available at https://github.com/cstein/GB-GA/tree/feature-glide_docking. SMILES strings, docking scores, and Molecule.one scores can be found at https://github.com/cstein/GB-GA_docking_supporting_information.

Supplementary Figures and Tables

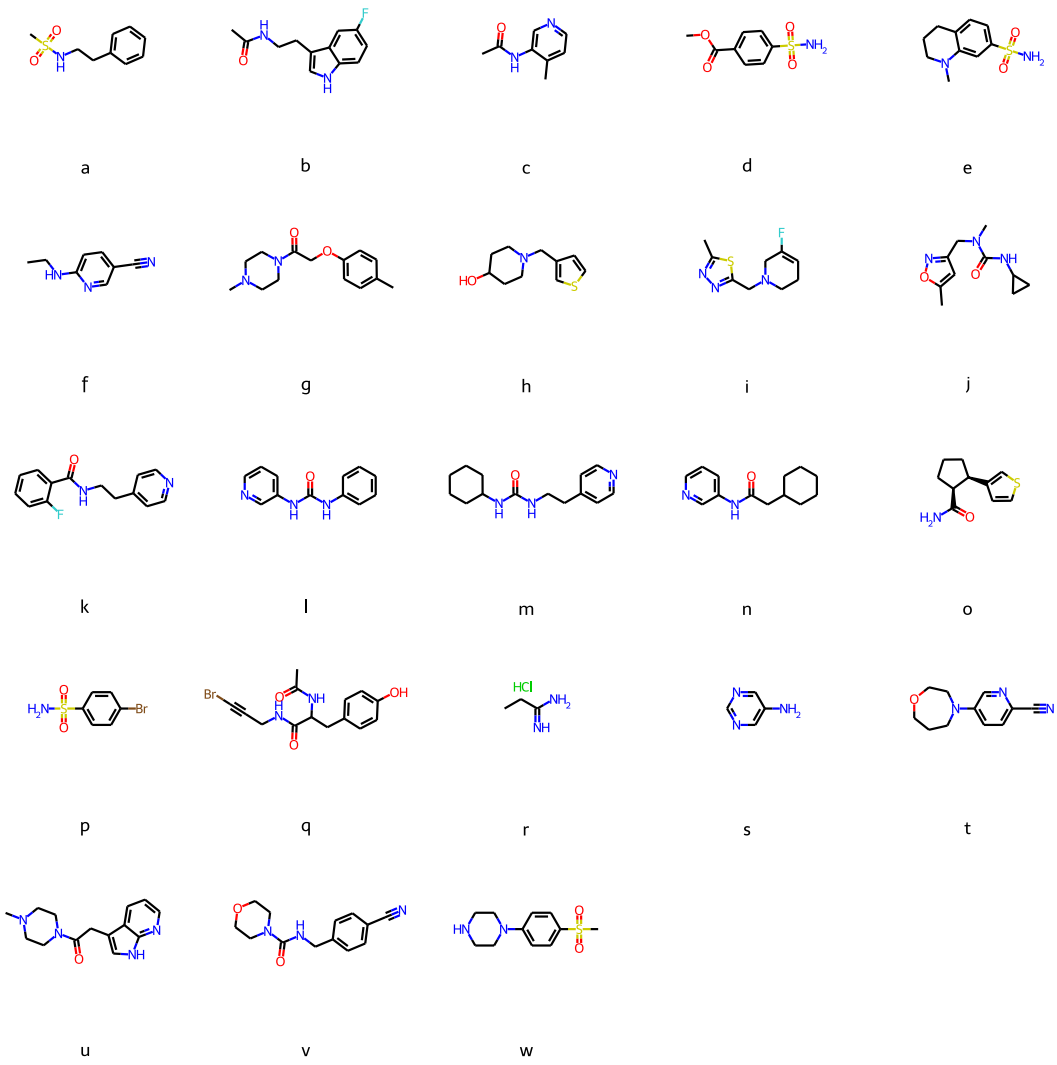

Figure S1. Fragments that bind non-covalently to M^{Pro} found by the COVID Moonshot organizers.[1] The organizers also found many covalently bound inhibitors that are not shown here.

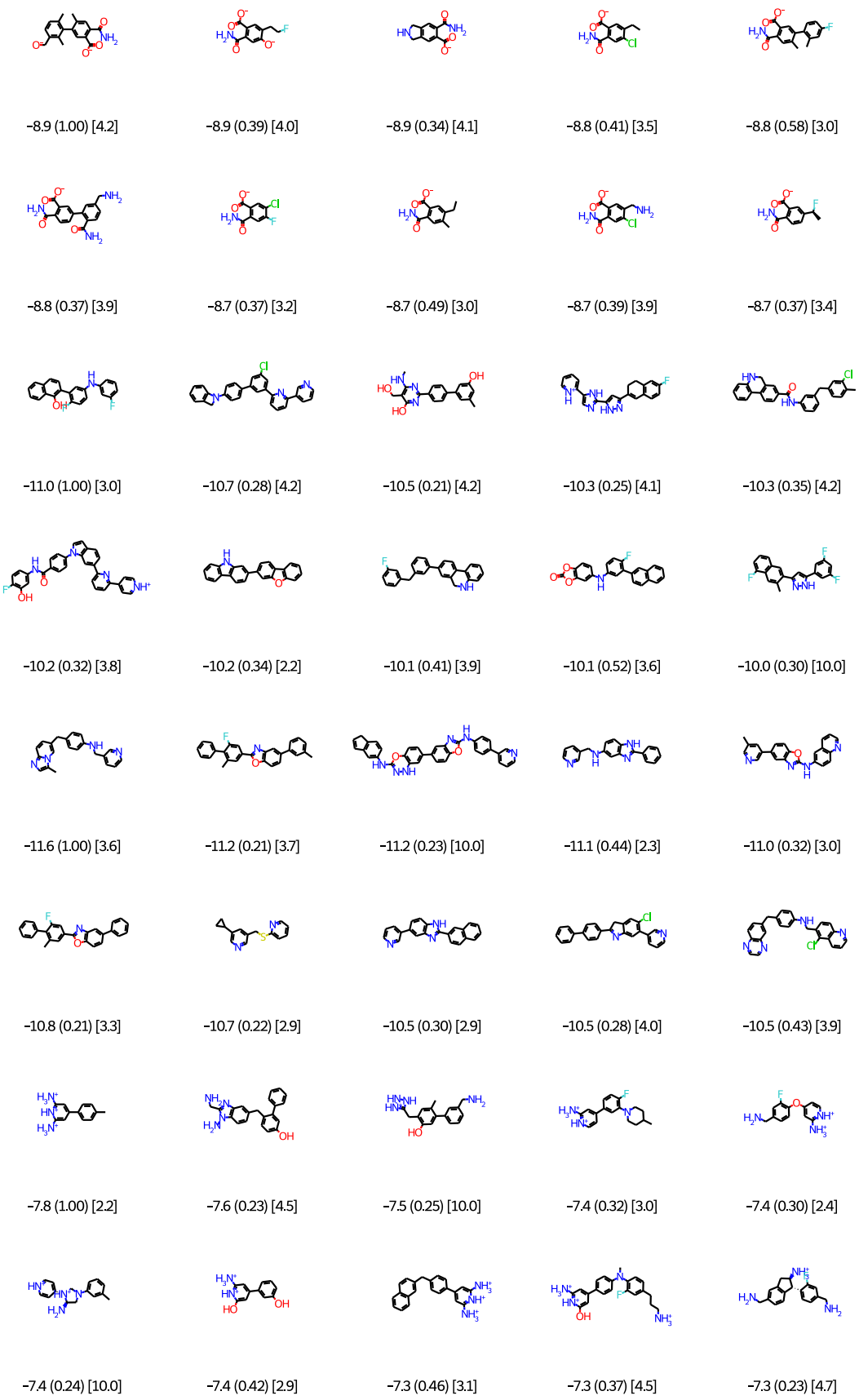

Figure S2. Top 10 scoring molecules obtained with GA+Filter+SA for each target (CM, β_2AR, DDR1, and BCD) together with the HTVS docking score, the ECFP4 Tanimoto similarity to the best scoring molecule (in parenthesis), and the Molecule.one score [in square brackets].

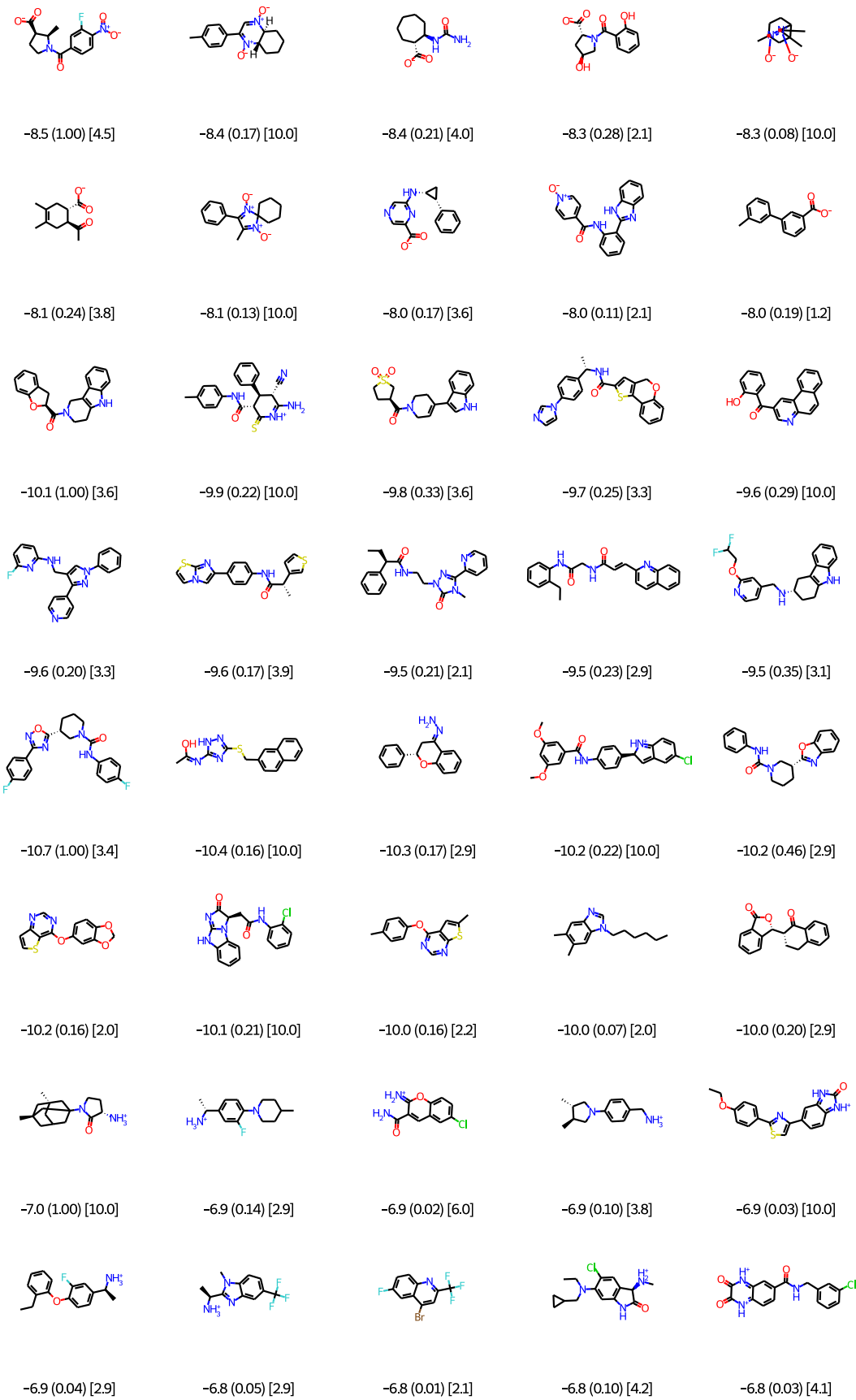

Figure S3. Top 10 scoring molecules obtained by screening the ZINC subset for each target (CM, β_2AR, DDR1, and BCD) together with the HTVS docking score, the ECFP4 Tanimoto similarity to the best scoring molecule (in parenthesis), and the Molecule.one score [in square brackets].

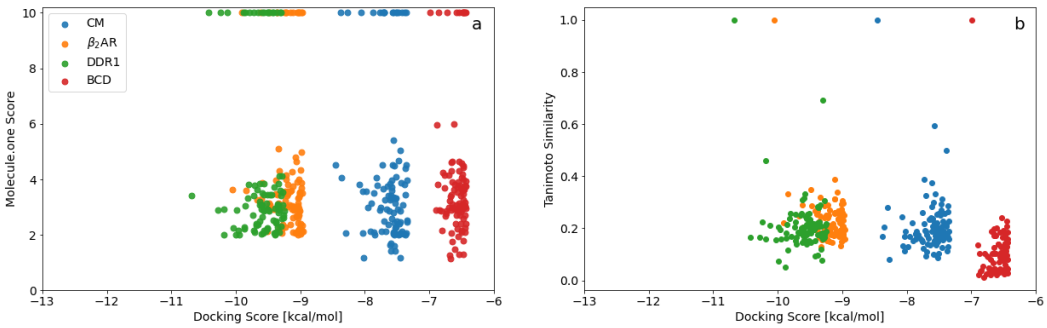

Figure S4. (a) Molecule.one score versus docking score for the 100 best binders predicted for the four different targets by screening the ZINC subset. (b) Tanimoto similarity to the best scoring molecule for each target vs docking score for the 100 best binders predicted for the four different targets by screening the ZINC subset.

REFERENCES

[1] A. Douangamath, D. Fearon, P. Gehrtz, T. Krojer, P. Lukacik, C. D. Owen, E. Resnick, C. Strain-Damerell, A. Aimon, P. Ábrányi-Balogh, J. Brandão-Neto, A. Carbery, G. Davison, A. Dias, T. D. Downes, L. Dunnett, M. Fairhead, J. D. Firth, S. P. Jones, A. Keeley, G. M. Keserü, H. F. Klein, M. P. Martin, M. E. M. Noble, P. O'Brien, A. Powell, R. N. Reddi, R. Skyner, M. Snee, M. J. Waring, C. Wild, N. London, F. von Delft, M. A. Walsh, *Nature Communications* **2020**, *11*, year.