Integrated Discovery in action: from Fragment Library to promising pan-coronavirus pre-clinical candidate

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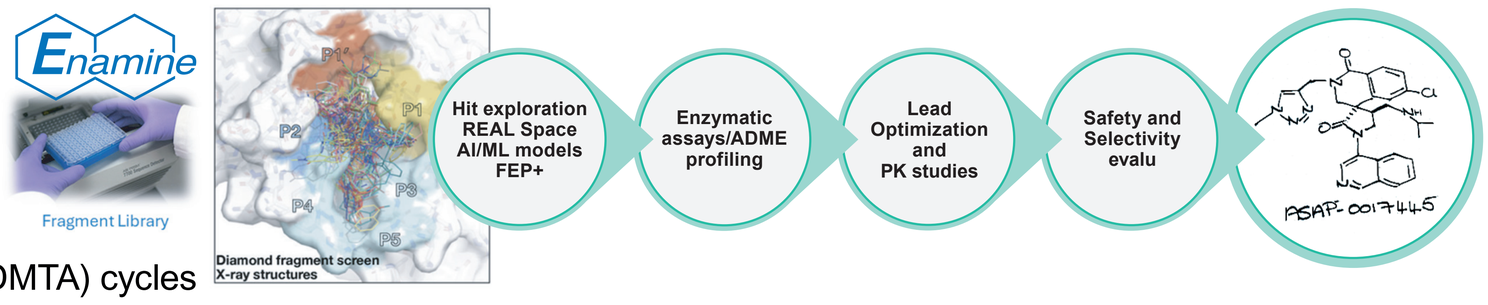
Introduction

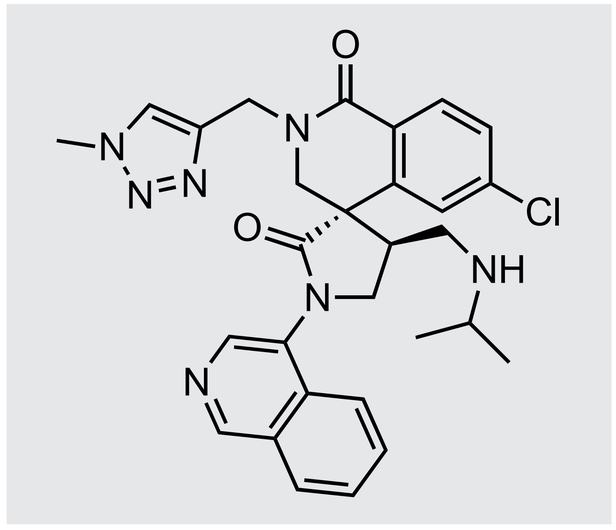
Rapid antiviral discovery is essential to address emerging coronavirus threats. We developed an integrated drug discovery platform combining Medicinal Chemistry, Synthesis, Enzymatic Assay, and ADME workflows to accelerate early-stage research. Operating within open-science collaborations such as COVID Moonshot and ASAP AViDD, the platform enables fast and cost-efficient progression from fragment hits to pre-clinical candidates. Through fragment-based screening, FEP+ based predictive modeling1, and high-throughput synthesis, we identified ASAP-00174452, a broad-spectrum, orally bioavailable antiviral active against SARS-CoV and MERS-CoV. Designed for global accessibility, ASAP-0017445 represents a promising candidate for future pandemic preparedness.

Methodology

- Target identification
- Fragment screening
- Computational design
- Parallel synthesis
- Biochemical and enzymatic assays.
- ADME and physicochemical profiling
- Iterative design-make-test-analyze (DMTA) cycles



Applications



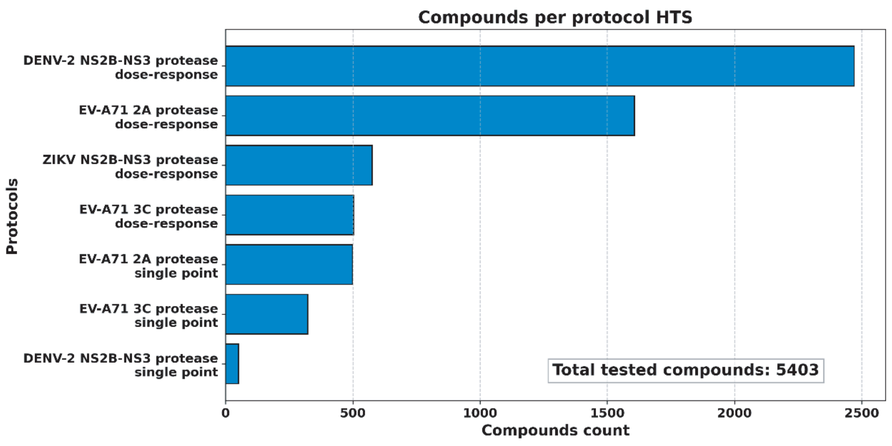
Targeting the highly conserved coronavirus main protease (M^{pro}) provides a promising strategy for developing broad-spectrum antivirals effective against SARS-CoV, MERS-CoV, and future coronaviruses. This approach supports pandemic preparedness by creating a platform for rapid therapeutic response, reducing dependence on time-consuming vaccine development. Through open-science collaborations such as COVID Moonshot and ASAP AViDD, compound libraries, structural data, and assay results are freely shared to accelerate antiviral research globally. The integrated workflow enables efficient lead optimization, resulting in potent and orally bioavailable protease inhibitors such as ASAP-0017445, which demonstrate strong safety and pharmacokinetic profiles. Designed for direct-to-generic access, these antivirals promote equitable global availability. Moreover, the collaborative and data-driven discovery model established here can be adapted to other viral families and infectious disease targets, broadening its impact beyond coronaviruses.

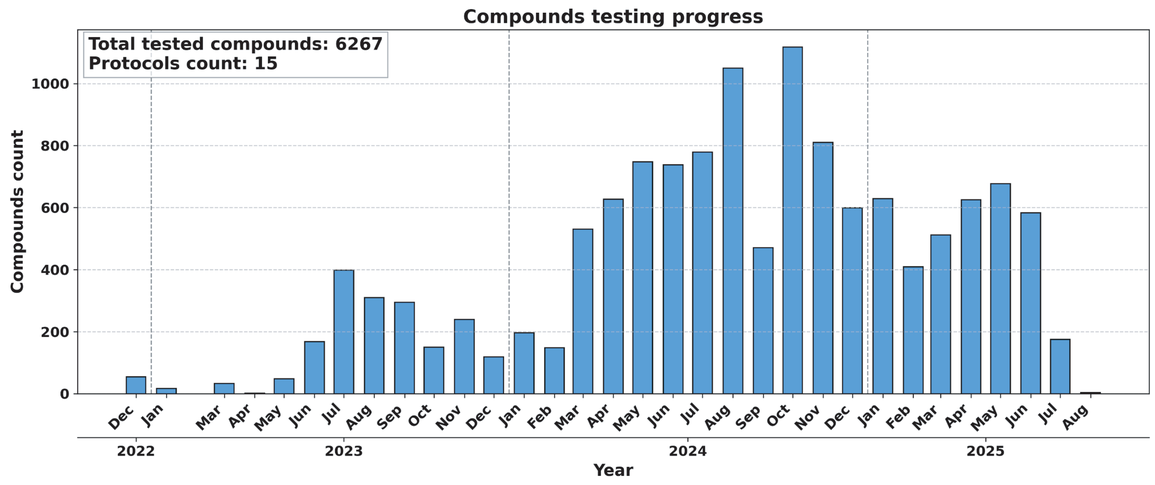
Results

The extensive high-throughput screening (HTS) campaign—covering over 6,000 compounds and multiple viral protease targets—provides a broad comparative dataset that strengthens the optimization of AS-0017445. Screening results from dengue, enterovirus, and Zika proteases enable the identification of cross-active scaffolds and structure–activity relationships that can guide refinement of AS-0017445 for broader antiviral potency.

The platform's iterative synthesis–assay–ADME workflow supports rapid analog generation and validation, helping to enhance the compound's selectivity, metabolic stability, and oral bioavailability. Furthermore, integrating new hits from related protease assays could reveal synergistic binding features applicable to coronavirus main protease inhibition.

Overall, these results extend the scope of AS-0017445 from a SARS/MERS-focused antiviral toward a unified, pan-viral protease inhibitor framework, reinforcing its potential as a globally accessible, next-generation antiviral candidate.





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References

* https://tinyurl.com/y3r7redd
1. https://www.choderalab.org/
2. Pan-coronavirus antiviral unveiled Laura HowesC&EN Global Enterprise 2025 103 (9), 6-6 DOI: 10.1021/cen-10309-scicon42.