molecule.one

Case Study

Accelerating Hit-to-Lead Campaigns with molecule.one's Focus Libraries

A pharmaceutical company ("Alpha"), a returning customer at this point, was running a hit-to-lead campaign using traditional approaches to create and screen focused libraries. They relied heavily on WuXi GalaXi and Enamine REAL virtual spaces to search for analogs of their hit molecules. Once compounds were selected, quotes were requested from WuXi or Enamine, and the compounds were synthesized.

However, this approach posed several challenges

Limited Diversity: Databases like Enamine REAL relied on decades of chemistry experience. This led to biased and fragmented chemical space, as the focus was on close analogs of prior successful syntheses, limiting true diversity.

Lack of Competitive Advantage: The widespread use of these databases meant competitors were accessing the same chemical space.

Slow Turnaround Times: The process often suffered from delays, significantly affecting project timelines.

molecule.one's solution

Advanced Feasibility Extrapolation: M1's AI models trained on M1's largest and fastest growing reaction dataset can extrapolate synthetic feasibility across a large diversity of building blocks, ensuring excellent predictions for compound synthesis.

Unexplored Chemical Space: M1's approach is novel, giving customers access to untapped regions of chemical space, providing a competitive edge.

Rapid Turnaround: First batch of compounds was delivered in just under four weeks.

Success-fee based model: M1 charged the customer only for compounds delivered successfully

The image shows our Head of Chemistry standing next to the stacked plates from what is likely the largest reaction screening campaign in this timeframe: **over 60,000 individual chemical reactions performed in just 14 days. This screen forms a portion of our fastest growing reaction dataset used to train models.**

Workflow and Results

The workflow was designed to closely mirror Alpha's existing processes. Alpha provided their scaffold and specified the vectors for expansion. For the first iteration, M1 designed a focused library of 157 compounds. When compared to databases previously accessed by Alpha (2.2M from WuXi and 40K from Enamine), the results were striking:

"[molecule.one's] chemistry already surpasses what we have been able to get from Enamine and WuXi. The diversity of your building blocks and chemistry is way better."

Building on this success, M1 used combined deep learning and chemical expertise to **design a focused library of ~20,000 analog compounds** centered around Alpha's scaffolds. M1 incorporated customer-requested filters on building blocks to increase the likelihood of identifying hit structures that would pass downstream PK tests.

Alpha virtually screened the library and requested a quote for 84 compounds. From this set, 46 compounds were selected for synthesis. M1 agreed to deliver these compounds in two batches, with the first batch shipped within four weeks. The first batch was drawn from SpaceM1, which is based on our proprietary HTE datasets; the second relied on literature data.

Outcome

In total, 32 compounds were synthesized and delivered on schedule, meeting Alpha's internal screening deadlines: 15/15 based on SpaceM1 and 17/31 based on literature data. By leveraging molecule.one's platform, Alpha significantly improved their screening library diversity, in a quicker turnaround time compared to their previous methods. **As a happy customer, Alpha has returned with a 2nd project (new pipeline) only a week after the 1st order was delivered.**