to biotechnology and pharmaceutical companies are ion channels and G-protein-coupled receptors, both of which have lately proven more amenable to x-ray crystallographic study. There is still much work to be done in terms of the design of fragment libraries. At present, we do not know with any certainty the optimum library size or the best way to maximize the potential of a library to generate chemical diversity during synthetic elaboration of fragment hits. Moreover, we do not yet know how best to screen fragment libraries. Various organizations have their respective biases, which reflect institutional memory, resource constraints, experience base, and the availability of particular skills, and so on. There is always the sobering possibility that fragment approaches will go the way of HTS, which appears to have fallen well short of expectations. We think it unlikely that fragment approaches will disappoint and we remain committed to exploring the potential of the method and continuously evolving our own process to maximize the likelihood of discovering development candidates suitable for entry into oncology clinical trials of targeted therapeutic agents.

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