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Generative AI platforms drive drug discovery dealmaking

Companies developing artificial intelligence-based platforms that enable the design of small-molecule and biologic drug candidates have been a focus of biopharma dealmaking in the past year.

Biopharma Dealmakers

Generative artificial intelligence (AI) burst onto the public stage in 2022 with the remarkable text-generating capabilities of the large-language model ChatGPT. Now, the potential of generative AI models to accelerate the design of drug candidates looks set to boost the funding raised in recent years by AI-focused companies and is driving dealmaking by major biopharma companies seeking to enhance their pipelines (Fig. 1 and Table 1, compiled using data provided by DealForma).

A case in point is Xaira Therapeutics, which emerged in April this year with \$1 billion of committed funding—one of the largest initial biotech funding rounds ever—and a high-profile management team. The company has the vision of end-to-end application of AI tools in drug research and development (R&D), including a class of generative AI tools called diffusion models to design biologic drugs such as antibodies. Generate Biomedicines, a company founded by Flagship Pioneering in 2018 that has raised around \$750 million since, is also applying such tools in antibody design.

On the dealmaking side, the potential to use generative AI tools to enable the design of antibodies for challenging targets such as membrane proteins or to identify drug candidates with best-in-class characteristics for established targets has been attracting large biopharma companies to partner with AI-focused companies. In November last year, Almirall announced a partnership with Absci potentially worth up to \$650 million to use its generative AI platform to identify antibodies for two therapeutic targets in dermatology (Table 1). The following month, Absci agreed another collaboration, this time with AstraZeneca to design an antibody drug candidate for an oncology target. Absci could receive up to \$247 million under the terms of the deal.

Absci is also pursuing its own candidates, with its first being an AI-designed antibody against the inflammatory disease target, tumor necrosis factor-like cytokine 1A (TL1A), which is currently in studies to support an investigational new drug (IND) application. The company is hoping to compete with the leaders in the race to bring a TL1A-targeted antibody to market for inflammatory bowel diseases, which has seen three large pharma companies—Merck & Co., Sanofi and Roche—all sign major deals in the past year or so to acquire or license a TL1A inhibitor in clinical development. In May 2023, Merck & Co. paid \$10.8 billion to acquire Prometheus Biosciences and its phase-3-ready TL1A-targeted antibody PRA023. Then, in October 2023, Sanofi and Teva announced a deal involving an upfront payment of \$500 million to Teva and up to \$1 billion in milestones around Teva's TEV-574, a TL1A-targeted antibody in phase 2 trials. Later the same month, Roche joined the fray when

it agreed to pay \$7.1 billion upfront and a near-term milestone payment of \$150 million to acquire Telavant and its phase-3-ready TL1A-targeted antibody RVT-3101.

Other AI companies involved in major deals recently include BigHat Biosciences, which entered a partnership with AbbVie with a headline value of \$355 million to develop therapeutic antibodies for oncology and neuroscience applications in December 2023 (Table 1). And in a deal potentially worth

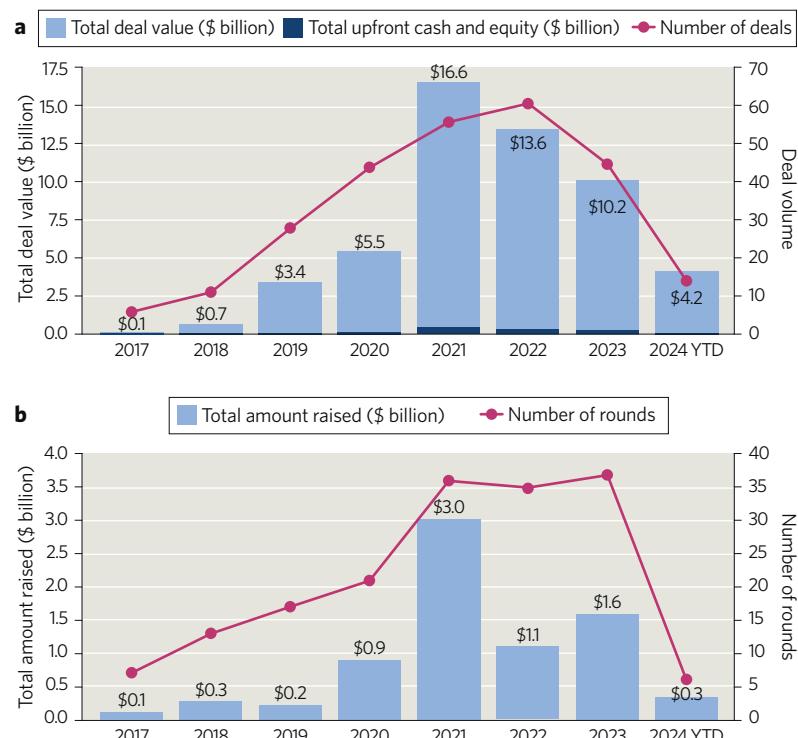


Fig.1 | Trends in deals and venture funding for companies engaged in AI/ML-enabled drug discovery and development. **a**, Drug discovery partnerships and service contracts. **b**, Venture funding. The DealForma database was filtered for licensing partnerships and service contracts focused on AI/ML-driven drug discovery. This included target identification, selection, protein design and related drug discovery programs, and excluded the use of AI/ML tools for non-therapeutic applications, clinical trial design, diagnostics, devices and so on. Source: DealForma, for the period from 1 January 2017 through to 29 March 2024. AI, artificial intelligence; ML, machine learning; YTD, year to date.

Table 1 | Selected recent partnership deals focused on applying AI in drug discovery

Date	AI-focused company; partner company	Deal summary
Biologic drug discovery		
5 December 2023	BigHat Biosciences; AbbVie	BigHat Biosciences signed a deal with AbbVie to use BigHat's AI-driven platform to develop therapeutic antibodies for oncology and neuroscience applications. AbbVie agreed to pay \$30 million upfront to BigHat, and BigHat is eligible to receive up to \$325 million in milestone payments, as well as sales royalties.
4 December 2023	Absci; AstraZeneca	Absci announced a collaboration with AstraZeneca to use its generative AI platform to design an antibody drug candidate for a specified oncology target. Absci could receive up to \$247 million, including an undisclosed upfront payment, R&D funding, milestone payments and sales royalties.
14 November 2023	Absci; Almirall	Almirall entered a partnership with Absci, which will apply its generative AI platform to identify therapeutic antibodies for two dermatological targets. Absci is eligible to receive up to \$650 million, including an undisclosed upfront payment, R&D funding and milestone payments.
10 October 2023	BioMap; Sanofi	BioMap agreed a collaboration with Sanofi to use BioMap's AI platform and Sanofi's biologics experience and data to co-develop AI models that enable biologic design and optimization. The deal included an upfront payment of \$10 million from Sanofi to BioMap, which is also eligible to receive more than \$1 billion in milestone payments for model development, as well as product-related R&D and sales milestones.
Small-molecule drug discovery		
13 February 2024	VantAI; Bristol Myers Squibb	Bristol Myers Squibb agreed to pay up to \$674 million to VantAI to apply the company's generative AI platform in the design of molecular glues for undisclosed therapeutic targets.
7 January 2024	Isomorphic Labs; Eli Lilly	Isomorphic Labs entered a strategic collaboration with Lilly to use its AI technology, including the next generation of AlphaFold, to discover small-molecule drug candidates for multiple undisclosed targets. Lilly agreed to pay \$45 million upfront and up to \$1.7 billion for meeting performance-based milestones.
7 January 2024	Isomorphic Labs; Novartis	Isomorphic Labs agreed to collaborate with Novartis on the discovery of small-molecule drug candidates for three undisclosed targets. Isomorphic received an upfront payment of \$37.5 million and is eligible to receive further milestone payments of up to \$1.2 billion.
4 January 2024	Insilico Medicine; Stemline Therapeutics	Stemline Therapeutics, a subsidiary of Menarini Group, signed a deal with Insilico Medicine to develop and commercialize a preclinical small-molecule inhibitor of the histone acetyltransferase KAT6A, designed using Insilico's generative AI platform, as a potential therapy for hormone-sensitive cancers and other cancer indications. Stemline agreed to pay \$12 million upfront to Insilico, and potential milestone payments could take the total value of the deal to more than \$500 million.
5 December 2023	Aqemia; Sanofi	Aqemia announced a collaboration with Sanofi using its platform based on generative AI and 'deep physics' to identify small-molecule drug candidates in several therapeutic areas. Under the terms of the agreement, Aqemia is eligible to receive up to \$140 million in upfront and milestone payments.
25 September 2023	Valo Health; Novo Nordisk	Valo Health and Novo Nordisk entered a collaboration to use Valo's Opal computational platform to discover and develop novel drugs for cardiometabolic disease. Novo Nordisk agreed to make an upfront payment and a potential near-term milestone payment worth \$60 million in total, and Valo is eligible to receive milestone payments of up to \$2.7 billion for up to 11 programs, as well as R&D funding and potential sales royalties.
20 September 2023	Exscientia; Merck KGaA	Exscientia and Merck announced a collaboration to use Exscientia's AI-driven drug-design capabilities to discover small-molecule drug candidates in oncology, immunology and neuroinflammation. Exscientia received \$20 million upfront and is eligible to receive up to \$674 million in milestone payments for three projects, as well as potential sales royalties.
20 September 2023	BenevolentAI; Merck KGaA	BenevolentAI and Merck entered a collaboration to use BenevolentAI's end-to-end AI platform to identify drug candidates for three targets in oncology, immunology and neurology. BenevolentAI is eligible to receive up to \$594 million, including an undisclosed upfront payment and milestone payments, as well as potential sales royalties.
12 September 2023	Insilico Medicine; Exelixis	Insilico Medicine agreed to license ISM3091, an IND-ready small-molecule inhibitor of the deubiquitinase USP1 identified using the company's generative AI platform, to Exelixis. Exelixis agreed to pay Insilico \$80 million upfront, and Insilico is also eligible to receive undisclosed milestone payments and royalties on sales.
30 May 2023	XtalPi; Eli Lilly	XtalPi announced a collaboration with Eli Lilly to use XtalPi's AI-supported platform for the de novo design of drug candidates for an undisclosed target. Eli Lilly agreed to pay up to \$250 million upfront and in milestones.

AI, artificial intelligence; IND, investigational new drug; R&D, research and development. Source: DealForma. The period analyzed was 1 January 2023 to 10 April 2024, and only deals with publicly disclosed information on the financial terms were considered for inclusion in the table.

more than \$1 billion between BioMap and Sanofi, announced in October last year, the companies will partner on the development of AI models to enable biologic design and development, such as BioMap's xTrimo, a large language model for protein structure prediction.

Sanofi also signed a deal with Aqemia in December around the application of generative AI for small-molecule drug discovery. Aqemia, which is eligible to receive up to \$140 million in upfront and milestone payments under the agreement, will collaborate with Sanofi using its platform based on generative AI and 'deep physics' to identify small-molecule drug candidates in several therapeutic areas (Table 1).

Another company involved in a duo of recent AI-related deals—announced on the same day in January at this year's JP Morgan conference—is Isomorphic Labs. The company was spun out of Google's DeepMind subsidiary in 2021 to work on drug discovery applications of AlphaFold, the AI-based protein structure-prediction tool that took the field by storm following its publication in 2021 (*Nature* **596**, 583–589; 2021). In one deal, Eli Lilly agreed to pay \$45 million upfront and up to \$1.7 billion in milestones to apply Isomorphic's technology to discover small-molecule drug candidates for multiple undisclosed targets. And in the other deal, Isomorphic received an upfront payment of \$37.5 million and is eligible to receive milestone payments of up to \$1.2 billion from Novartis to work on drug candidates for three undisclosed targets.

September saw another same-day announcement of two AI-related collaborations, in this case set up between Merck KGaA and two AI-focused companies, Exscientia and BenevolentAI (Table 1). The deal with Exscientia is focused on applying this company's AI-based drug design capabilities to identify small-molecule drug candidates in the oncology, immunology and neuroinflammation areas, and the terms include a \$20 million upfront payment to Exscientia and up to \$674 million in milestone payments, as well as potential royalties on resultant products. The partnership with BenevolentAI is

aiming to apply their platform to discover drug candidates for three targets in oncology, immunology and neurology. In this case, the potential value of the deal could be up to \$594 million, including an undisclosed upfront payment to BenevolentAI and milestone payments. Sales royalties on commercialized products would also be payable.

Insilico Medicine, one of the pioneers in the application of generative AI in small-molecule drug discovery, has also signed a couple of major deals in the past 12 months (Table 1). In September 2023, the company agreed to license an IND-ready small-molecule inhibitor of an anticancer target, the deubiquitinase ubiquitin carboxyl-terminal hydrolase 1 (USP1), to Exelixis for \$80 million upfront. Insilico Medicine is also eligible to receive milestone payments and royalties on future sales. This was followed by another deal for a preclinical small-molecule inhibitor for an anticancer target in January 2024, this time the histone acetyltransferase KAT6A, with Stemline Therapeutics. The total potential value of the deal to Insilico Medicine could be more than \$500 million, including an upfront payment of \$12 million.

Insilico Medicine made the news this year as well with a publication around its leading pipeline candidate INS018_055, a small-molecule inhibitor of the novel antifibrotic target TRAF2- and NCK-interacting kinase (TNIK), which was also identified using the company's end-to-end platform (*Nat. Biotechnol.* (2024); doi:10.1038/s41587-024-02143-0). The compound is currently in a phase 2 trial for idiopathic pulmonary fibrosis—an indication for which new therapies are greatly needed and that has historically seen many failures in drug development.

While AI-designed antibodies are yet to reach the clinic, the outcomes from trials for small molecules such as INS018_055 that are now in progress will be closely watched to understand whether AI is able to accelerate not just the discovery of drug candidates, but also the identification of those that are capable of succeeding in the clinic where others have not in the past.