# A complex path forward

## 2023 Beyond Borders report, Texas edition

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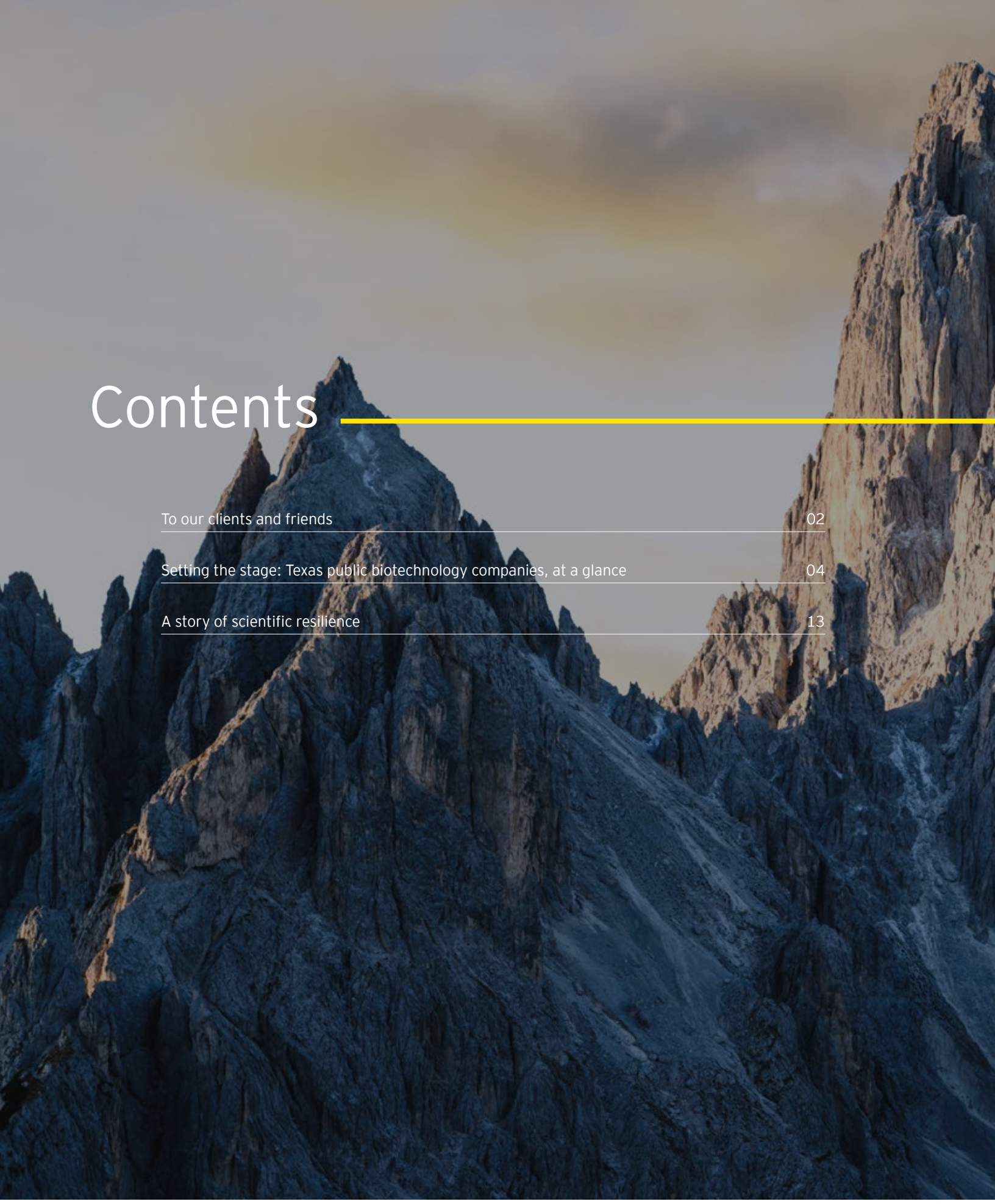

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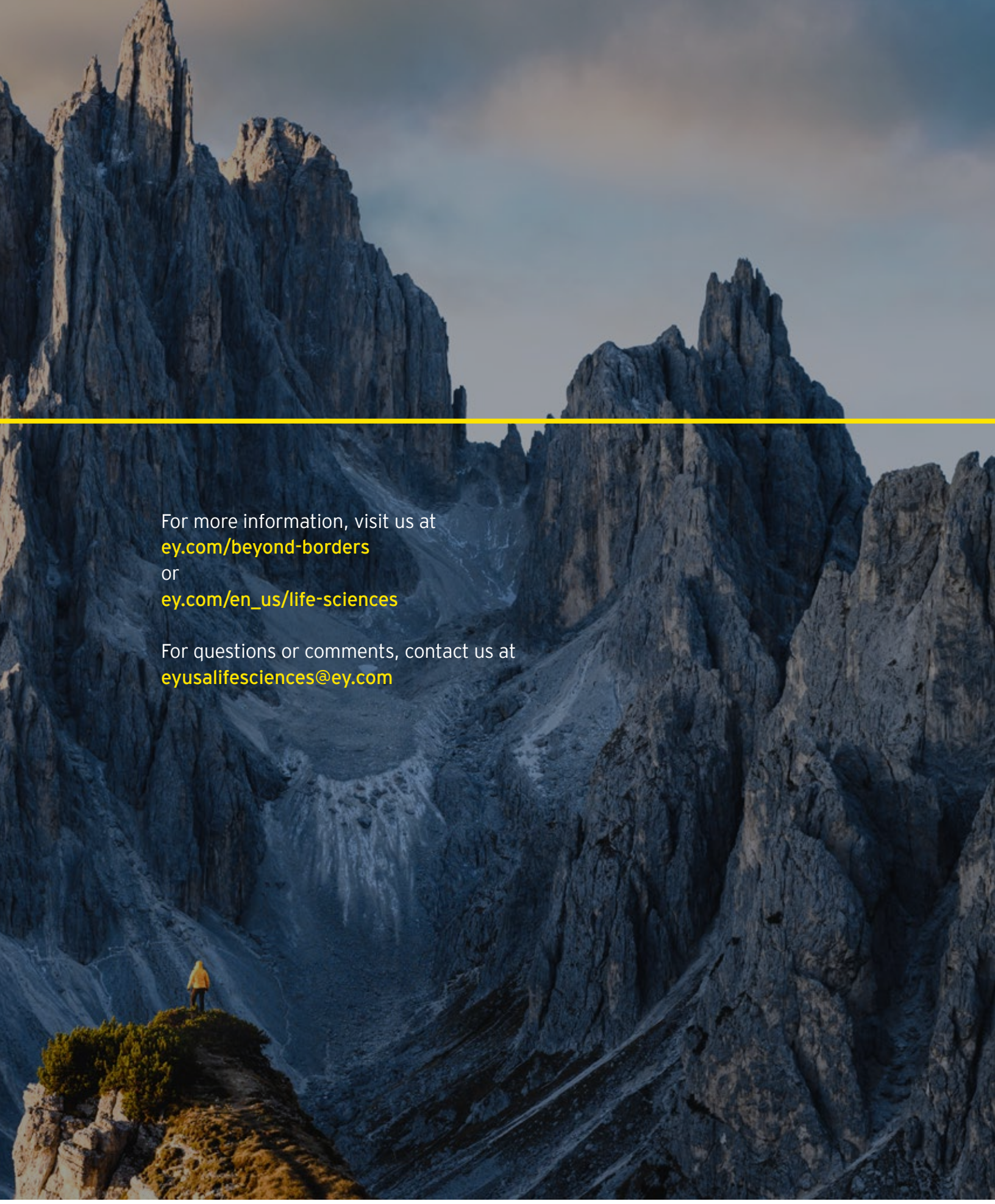

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# To our clients and friends

The 33rd edition of our Beyond Borders report sees the US and European biotechnology (biotech) sector seeking a new path forward. At the time of initial publication in mid-2023, the priorities of biotech companies varied based on the level of their commercial maturity. Today, biotech commercial leaders (companies with at least US$500 million in annual revenue), along with their big pharma counterparts, remain in dire need of addressing innovation deficits and creating new revenues to offset the massive wave of pending patent expirations. On the other end of the spectrum, emerging biotechs continue to face a capital-constrained operating environment and are wholly focused on getting to the next value inflection point with minimal cash burn. However, the handful of fortunate emerging biotechs with de-risked, late-stage assets will likely attract lucrative multiples for partnering or outright acquisitions. These dynamics together mean a complex path forward for the biotech sector as a whole.

The biotech sector must navigate this complex path forward by driving efficiencies and streamlining its core operations, from research and development to supply chain to commercial operations, while trying to maximize organic and inorganic growth through the use of M&A and alliances. Despite these challenges, biotech's deep capabilities around innovation and the importance of its product offerings mean the sector still maintains a favorable mid- to long-term outlook. Companies that focus on the fundamentals will be poised to lead the next phase of expansion once the impact of the recessionary environment and tighter monetary policies subsides.

Amid surging product demand and investor focus on the sector, biotech performed extraordinarily well during the early waves of the global chaos caused by the COVID-19 pandemic by attracting an influx of new capital. By early 2022, however, the stimulus to the biotech market was fading fast. In the previous edition of this report, we wrote: "the financial environment for biotech has significantly shifted in the opening months of 2022, with valuations plunging and the IPO window closing." This shift has since continued and intensified, with biotech now facing reduced capital availability in a landscape of higher interest rates, tightening credit conditions, and broader macroeconomic and geopolitical disruption. Moreover, the sector is bracing for a tougher pricing environment in the wake of the US Inflation Reduction Act (IRA), with significant implications for how the sector will secure reimbursement for its innovation in the future. By all measures, from revenues to financing, M&A investment and beyond, biotechs experienced declining performance and increasing challenges in 2022.

However, despite these challenges, the sector as a whole remains robust. Biotech R&D continues to fuel an innovation renaissance in new biopharma products and platforms, and the pandemic emergency served to highlight the strategic importance of the sector to national and international health and security. As always, there will be winners and losers within the sector. Good science leading to differentiated products will always be the key to success in this R&D-driven sector, but as they plan ahead, biotechs need to recognize the need to supplement scientific excellence with a strategic focus on achieving operational efficiency in all areas of the business.

The life sciences have changed beyond all recognition over the past century; yet the rate of change is now accelerating, as the technologies to enable a data-driven intelligent health ecosystem to begin to penetrate the sector. As companies seek the right model for future growth, they must also be mindful of this underlying turn toward a digitalized, data-driven, personalized care system. Companies that can best adapt to the current changing conditions, combining cutting-edge innovation with a newly sharpened focus on efficiency and resilience in business fundamentals, will emerge from the downturn strengthened and in a position to drive the next wave of growth for the biotech sector as it evolves toward a smarter, more personalized future.

For Texas biotechs, which saw total revenue of US$203.5 million last year, 2023 so far has been marked by a partial rebound, increased R&D spending and measurable progress around FDA product approvals. While investment into the sector remains slow across the Lone Star State in 2023 compared to previous years, many sector watchers believe that slowing interest rate hikes may be imminent, which could position more mature biotechs well for the resurging investment activity expected to take place as a result. Early-stage players, however, should consider supplementing their scientific excellence with a strategic focus on achieving operational efficiency and resilience in all areas of the business, as 75% of emerging Texas biotechs lack adequate funds to continue their operations beyond a further two years. All told, these conditions are contributing to a climate of cautious optimism for the sector in Texas, and we believe the below data serves to validate that perspective.

# Setting the stage: Texas public biotechnology companies, at a glance

**Figure 1. Texas public biotechnology companies, at a glance (US$m)**

| | H1 2023 | 2022 | 2021 | % change (2022-21) |
|---|---|---|---|---|
| Public data company | | | | |
| Revenues | 180.3 | 203.5 | 238.3 | -15% |
| R&D expense | 643.6 | 1,154.1 | 1,042.2 | 11% |
| Net income | -843.4 | -1,806.2 | -1,497.9 | 21% |
| Market capitalization | 7,208.2 | 5,044.6 | 4,985.3 | 1% |
| Number of employees | - | 1,774 | 1,494 | 19% |
| Financing | | | | |
| Capital raised by public companies | 418.9 | 356.6 | 1,768.7 | -80% |
| Number of IPOs | - | 2 | 3 | -33% |
| Number of companies | | | | |
| Public companies | 28 | 28 | 26 | 8% |

Sources: Source: EY analysis, Capital IQ and company financial statement data.

- Public Texas biotech firms experienced a 15% decline from 2021 to 2022 in total revenues following the significant surge in sector sales driven by the pandemic in 2021. However, revenues increased in the first half of 2023 and are on track to double those of 2022. This partial rebound in 2023 is primarily propelled by the substantial contributions of Castle Biosciences, Molecular Templates and Reata Pharmaceuticals, which together accounted for 88% of total revenue in H1 2023 for the state's biotech sector.
- Meanwhile, research and development expenses increased by 11% for Texas biotechs due to their reinvestment of profits into R&D efforts.

Among the publicly traded Texas biotech companies that generated product revenue, only Castle Biosciences managed to boost both its top- and bottom-line growth. In contrast, the rest of the publicly traded biotech firms in Texas have predominantly depended on revenue streams stemming from government grants, collaboration agreements and licensing arrangements. Despite this, the outlook for the remainder of 2023 is optimistic, with revenue poised to increase following FDA product approvals for two Texas biotech companies, Reata Pharmaceuticals and Lexicon Pharmaceuticals. In addition, other biotechs in the state are expected to launch and successfully market their flagship products this year.

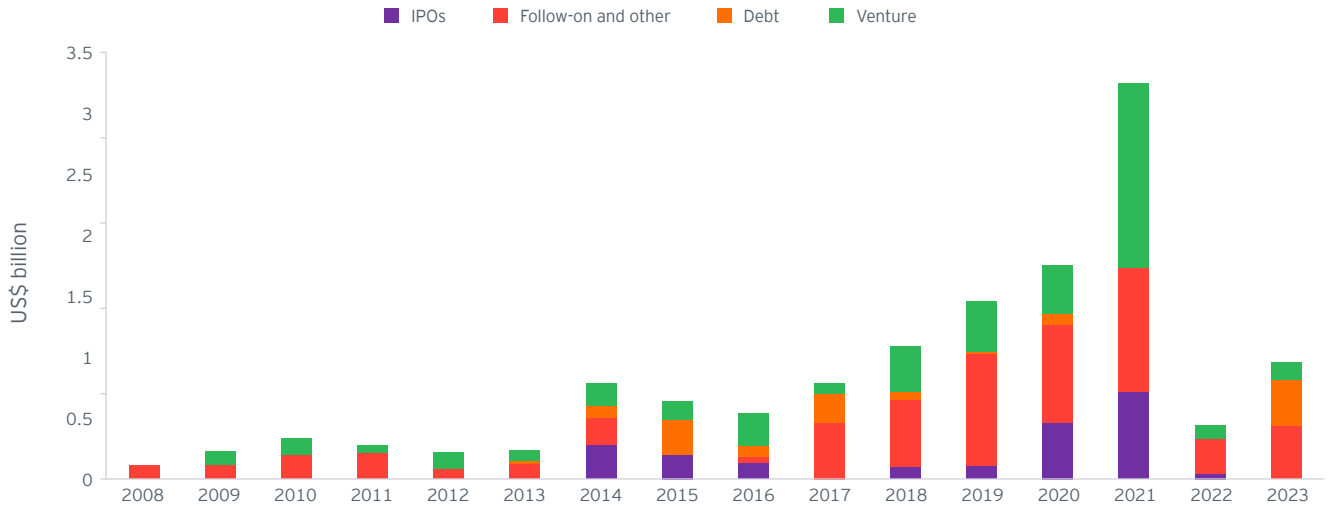
**15%**

decline in total revenues from 2021 to 2022 for Texas biotechs

**11%**

increase in R&D expenses from 2021 to 2022 for Texas biotechs

Figure 2: Behind the scenes: funding the growth of Texas biotechs, 2008–23




Sources: EY analysis, Capital IQ and VentureSource.

**86%**

decrease in total funding from 2021 to 2022 for Texas biotechs

**61%**

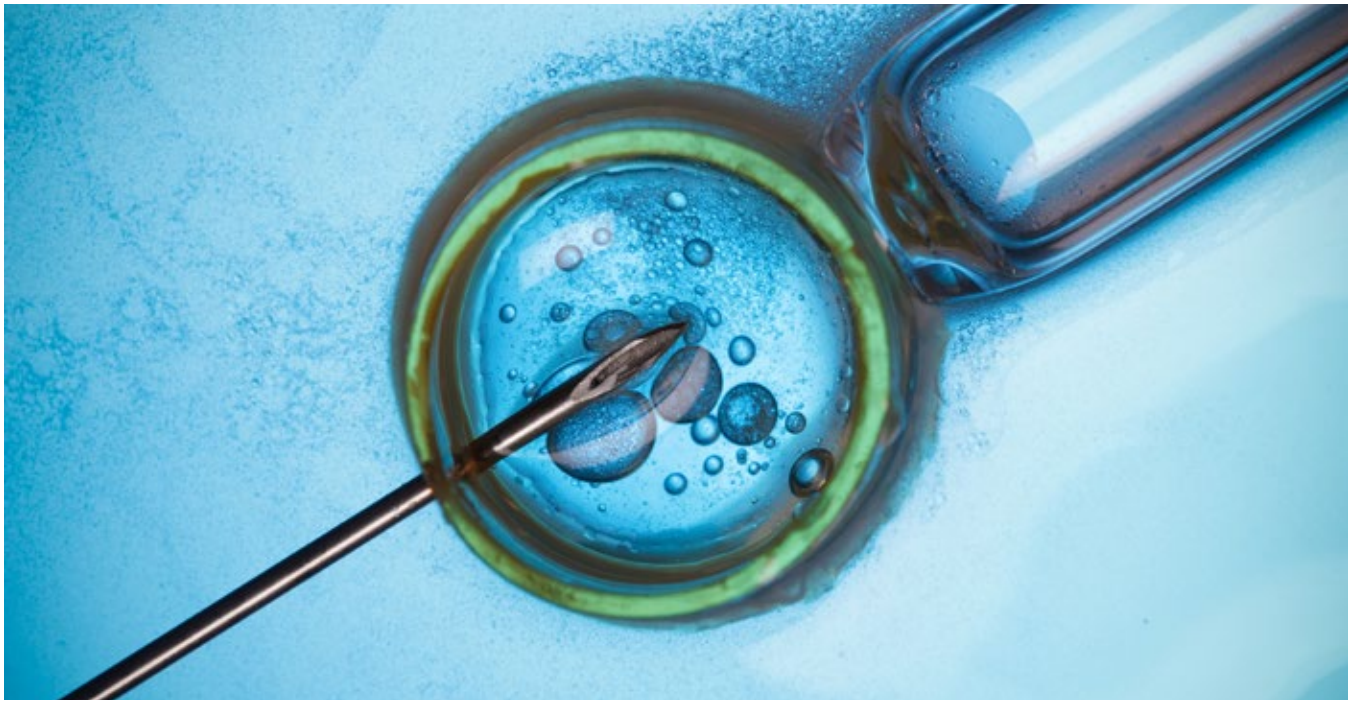
of 2022 follow-on funding total for Texas biotechs raised in Q4

While public company data tells part of the Texas sector's story, there is also a large group of private biotechs fueling new scientific solutions. The amount and type of financing for both public and private biotech entities reflect the sector's willingness to invest in Texas biotech innovation. Figure 2, above, shows the capital raised by Texas biotech companies for each of the years from 2008 through the first half of 2023, broken out between IPOs, follow-on and other financing, debt, and venture capital investment.

As we mentioned in our 2022 report, funding of Texas biotech companies was unprecedented in 2021, with one of the largest venture fundings in the history of the sector, as well as one of the largest biotech IPO raises of the year — and with nearly US$729 million raised through IPO financing.

From 2021 to 2022, however, Texas saw a total funding decrease of 86%. Specifically, Texas biotech companies experienced a decline of 73% in the capital raised through follow-on public offerings, a 97% decrease in capital raised through the IPO market, and a 91% drop in capital raised through venture funding.

In addition, over half of the total 2022 investment in the sector in Texas came in the second half of the year (68% of the total). The majority of this funding came from follow-on investment, followed by venture capital and a small amount of IPO proceeds. Of the follow-on total, 61% was raised in the fourth quarter of 2022 alone, with US$109.4 million coming over the first nine months of that year.



Out of the eight Texas companies that underwent public offerings in 2020 and 2021, six witnessed a decrease in their market value by the conclusion of 2022, marking an average decline of 79%. Coupled with the significant downturn in follow-on funding, these headwinds may create material operational challenges for these recently launched enterprises.

Apprehensions about enduring viability span beyond newly public biotechs to the broader sector in Texas. Analysis indicates that as of 2022, 75% of emerging Texas biotech firms (i.e., companies with less than US$500 million in annual revenue) lacked adequate funds to continue current operations past two years, while 39% had less than one year's worth of cash remaining.

Despite 2022's negative trends compared to the peak years of 2019, 2020 and 2021, financing levels in 2022 were impressive from a broader historical perspective. In the five-year period following the onset of the financial crisis in 2007, Texas companies raised on average US$238.2 million annually. The subsequent decade from 2013 to 2022 has seen average investment surge to US$1.1 billion annually. Aside from IPO investment (which last year sank to its lowest level since 2017), the financing picture in the first half of 2023 aligned far more closely with the rest of the decade, with Texas biotechs already raising a sum of US$978.4 million in funding as of June 30, 2023, more than doubling the total financing secured in all of 2022.

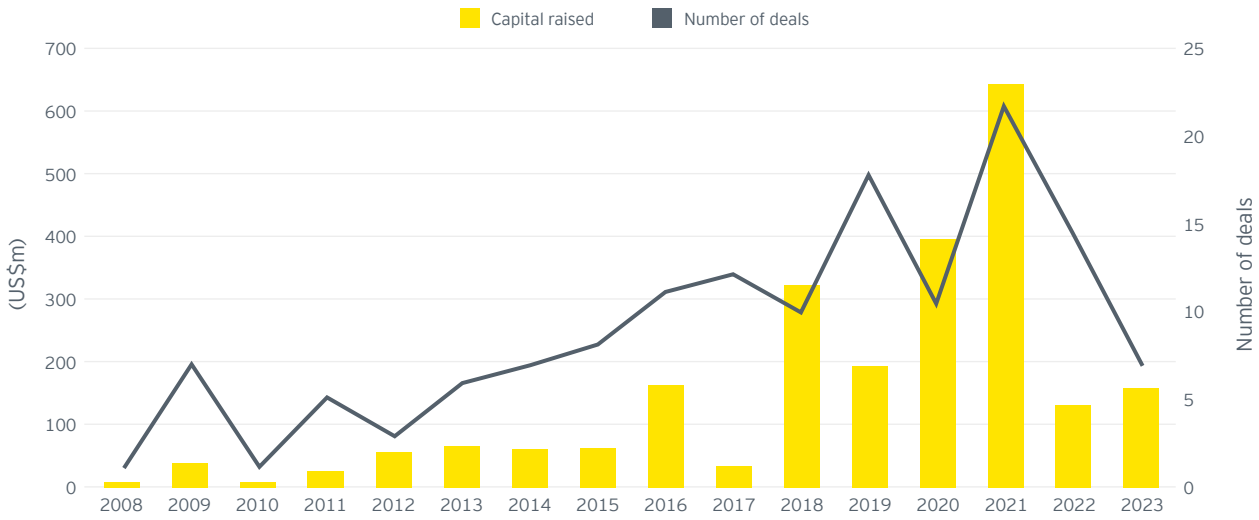
**US$978.4m**
decrease in total funding from 2021 to 2022 for Texas biotechs

The first several months of 2023 saw a change in the mix of financing for Texas biotechs, away from venture and IPO financing in 2021 and an increase in debt financing. While debt financing may allow companies to raise capital without dilution — often important to early-stage entities — it can be expensive, especially with rising interest rates and a constrained capital market. Additionally, biotechs and their investors continue to be impacted by a string of bank failures, most notably by Silicon Valley Bank (SVB), the bank of choice for many in the biotech sector. While a catastrophe was largely avoided, early-stage biotechs need to revisit their liquidity policies and diversify their banking strategies. SVB's collapse has taught biotechs to spread their money across multiple startup-friendly banks rather than relying on only one. The bank's demise also leaves smaller biotechs without an alternative lender since many other banks have raised their funding thresholds to points that make investment difficult for smaller entities. SVB's absence may mean that fewer companies receive financing, and some biotechs may need to pare back pipelines of medicines in development. However, those companies with sound management and strong pipelines will continue to be funded.

The constrained financing environment for small biotechs, particularly those focused on new modality platforms, highlights the importance of M&A for biotech. With lower capital availability, the obvious exit route for biotechs is to seek acquisition. However, the sector's larger players had little appetite for major dealmaking in 2022, with M&A investment increasing slightly compared to 2021 but still well below the levels witnessed between 2018 and 2020. That said, in July 2023, Texas witnessed a major transaction as Biogen announced its proposed acquisition of Reata Pharmaceuticals for US$7.3 billion, enabling access to Skyclarys (omaveloxolone), an innovative FDA-approved Friedreich's ataxia treatment. Through this acquisition, Biogen aims to synergize Skyclarys' commercialization with Spinraza (for spinal muscular atrophy) and Qalsody (for amyotrophic lateral sclerosis (ALS)).[1]

1. "Biogen, amid layoffs, ponies up $7.3B for rare disease specialist Reata and potential blockbuster Skyclarys," Fierce Pharma website, https://www.fiercepharma.com/pharma/biogen-ponies-73b-rare-disease-specialist-reata-and-potential-blockbuster-skyclarys#:~:text=Four%20days%20later%2C%20Biogen%20has,you%20guessed%20it%E2%80%94%247.3%20billion., 28 July 2023.

## Figure 3. Texas early-stage venture investment




Sources: EY analysis, Capital IQ and Dow Jones VentureSource.

- Despite the drop in venture spending overall, it was notable that US$134 million (95% of total venture funding in Texas biotechs in 2022) went to early-stage companies (i.e., to seed, first or second financing rounds). Though the total of 14 early-stage deals in 2022 was down compared to 2021, it was slightly above the whole-decade average of 12 early-stage deals. Further, the first half of 2023 has already seen 7 early-stage deals.
- During the initial six months of 2023, early-stage venture companies in Texas have already secured approximately US$160 million in funding, reflecting a 19% increase compared to the total funding of $134 million for the entire year of 2022.
- It must be noted, however, that 37% of the early-stage total came from the US$50 million first-round investment in Indapta Therapeutics of Houston, Texas.

**95%**

of total venture funding in Texas biotechs in 2022 went to early-stage companies

**US$160m**

in funding secured by early-stage Texas biotechs in H1 2023

## Figure 4. Top Texas venture rounds of 2022 and the first half of 2023

| Name | Therapeutic focus of lead candidate | Clinical stage of lead candidate | Gross raised (US$m) | Year | Quarter | VC round type |
|---|---|---|---|---|---|---|
| Colossal Biosciences Inc. | Other | N/A | $150 | 2023 | Q1 | Early |
| Indapta Therapeutics Inc. | Cancer | Phase 1 | $50 | 2022 | Q1 | Early |
| RadioMedix, Inc. | Cancer | Approved | $40 | 2022 | Q4 | Early |
| Systemic Bio | Cardiovascular | N/A | $15 | 2022 | Q3 | Early |
| Phantom Neuro Inc. | Orthopedic | N/A | $9 | 2022 | Q3 | Early |
| Cao Pharmaceuticals Inc. | Cancer | Phase II | $5 | 2022 | Q2 | Early |
| FibroBiologics, Inc. | Multiple | N/A | $5 | 2023 | Q1 | Early |
| Aperiam Bio, Inc. | Other | N/A | $4 | 2022 | Q1 | Early |
| Pulmotect, Inc. | Respiratory | Phase II | $2 | 2022 | Q1 | Early |

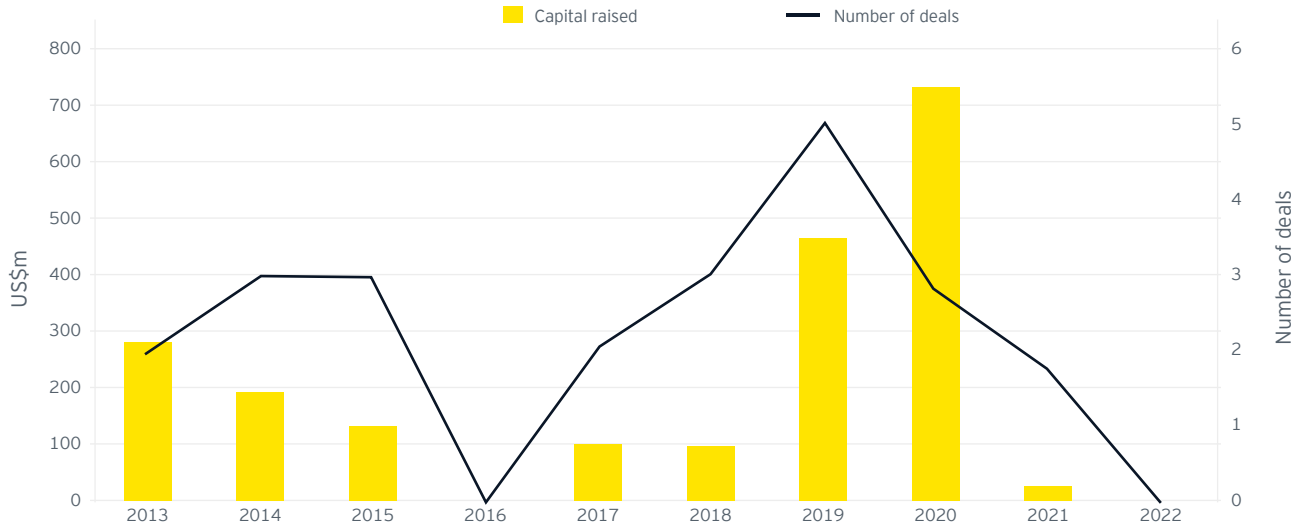
Sources: EY analysis, Capital IQ.

Similar to past years, the largest share of biotech venture funding in Texas in 2022 was garnered by companies that are focused on the field of oncology.

- Similar to past years, the largest share of biotech venture funding in Texas in 2022 was garnered by companies that are focused on the field of oncology. Among them was the most significant venture funding of the year, accomplished by Indapta Therapeutics, which secured a substantial sum of US$50 million. This funding infusion aims to further propel the development of its universal, allogeneic NK cell platform toward an Investigational New Drug (IND) Application and subsequent clinical trials.
- The second-largest biotech funding round in Texas in 2022 was accomplished by RadioMedix, as the company successfully raised US$40 million. This funding injection is designated to further advance the development of AlphaMedix™, a pioneering lead-212 ($^{212}$Pb) labeled somatostatin analogue Targeted Alpha Therapy (TAT) agent, aimed at addressing the treatment needs of metastatic or inoperable somatostatin-expressing neuroendocrine tumors.[2]

2. "212Pb: Production Approaches and Targeted Therapy Applications," National Institutes of Health website, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8777968/, 13 January 2022.

## Figure 5. Texas biotechnology IPOs by year




Sources: EY analysis, Capital IQ and VentureSource.

- As noted above, the record-breaking Texas biotech IPO market of 2021, which raised US$729 million in investment, disappeared almost entirely in 2022, with only US$25.1 million generated in biotech IPO revenue. This total was the lowest since 2018, as was the number of IPOs (two) and the average round size (US$12.5 million). This activity reflects the fact that many generalist investors turned away from the sector, resulting in a plunge in valuations.[3] Rather than seeking an early IPO, Texas biotechs can now be expected to prolong the capital raised in early venture capital (VC) rounds or pursue additional private funding (or seek other alternatives such as reverse mergers) before attempting a public market debut.
- The shift away from biotech as a focus for investment means that the IPO market is now in much the same position it was a decade ago, dependent on specialist investors (as described at the time in the 2013 *Beyond Borders* report). Nevertheless, the hope is that with slowing interest rate hikes, a rebalanced IPO market may recover in the near future, with the focus back on fundamentals, including clinical validation of assets.

3. "Biopharma and Medtech Review 2021," Evaluate website, https://info.evaluate.com/rs/607-YGS-364/images/jn371-vantage-2021-review-report.pdf, February 2022.

## Figure 6. US and European IPOs, 2022

| Name | Region | Therapeutic focus of lead candidate | Clinical stage of lead candidate | Gross raised (US$m) | Quarter |
|---|---|---|---|---|---|
| Third Harmonic Bio | US – Massachusetts | Multiple | Preclinical | $238 | Q3 |
| HilleVax | US – Massachusetts | Infectious disease | Phase II | $230 | Q2 |
| Prime Medicine | US – Massachusetts | Multiple | Preclinical | $175 | Q4 |
| ArcellX | US – Maryland | Oncology | Phase II | $142 | Q1 |
| PepGen | US – Massachusetts | Neurology | Phase I | $108 | Q2 |
| Vigil Neuroscience | US – Massachusetts | Neurology | Phase I | $98 | Q1 |
| Acrivon Therapeutics | US – Massachusetts | Oncology | Phase II | $94 | Q4 |
| AN2 Therapeutics | US – Northern California | Respiratory | Phase II/III | $79 | Q2 |
| Aelis Farma | France | Neurology | Phase II | $28 | Q1 |
| Blue Water Vaccines | US - Ohio | Infectious disease | Preclinical | $20 | Q1 |
| TC Biopharm | UK | Oncology | Phase I | $18 | Q1 |
| Coya Therapeutics | US – Texas | Multiple | IND-enabling | $17 | Q4 |
| Nuvectis Pharma | US – New Jersey | Oncology | Phase I | $16 | Q1 |
| Hillstream Biopharma | US – New Jersey | Oncology | IND-enabling | $15 | Q1 |
| MAIA Biotechnology | US – Illinois | Oncology | Phase II | $10 | Q3 |
| Bullfrog AI | US – Maryland | Oncology | Phase I | $8 | Q4 |
| bioAffinity Technologies | US – Texas | Oncology | Unknown | $8 | Q3 |
| Lipella Pharmaceuticals | US – Pennsylvania | Women's health | Phase II | $7 | Q4 |
| Genflow Biosciences | UK | Genetic | Preclinical | $5 | Q1 |
| OKYO Pharma | UK | Ophthalmic | Phase I | $3 | Q2 |

Sources: EY analysis, Capital IQ and Dow Jones VentureSource.

- Of the two Texas IPOs in 2022, the largest by value was carried out by Coya Therapeutics, Inc., which raised US$17.3 million. The company's lead asset is a treg-enhancing/T effector and macrophage depleting biologics combination (for ALS) currently seeking proof-of-concept data.[4]
- The second Texas IPO was raised by bioAffinity Technologies, Inc (US$7.8 million) to expand existing operations and commercialization of bioAffinity's core product – CyPath® Lung, used to diagnose early-stage lung cancer – to support the development of additional diagnostics and cancer therapeutics.[5]
- If the pace of interest rate hikes slows, some small privately held biotech companies, including Texas startups, may be positioned for a resurgence in IPO activity during the latter part of 2023. Nevertheless, the prevailing challenging economic circumstances are expected to influence investors to favor companies that are already engaged in human trial drug development.[6]

4. "Coya Therapeutics, Inc. Provides Business Update and Reports Q1 2023 Unaudited Financial Results," *Coya Therapeutics website*, https://ir.coyatherapeutics.com/news/news-details/2023/Coya-Therapeutics-Inc.-Provides-Business-Update-and-Reports-Q1-2023-Unaudited-Financial-Results/default.aspx, 10 May 2023.
5. *bioAffinity website*, https://bioaffinitytech.com/.
6. "Analysis: Biotech IPOs to bloom with spotlight on startups with human trial data," *Reuters website*, https://www.reuters.com/markets/deals/biotech-ipos-bloom-with-spotlight-startups-with-human-trial-data-2023-02-13/, 13 February 2023.

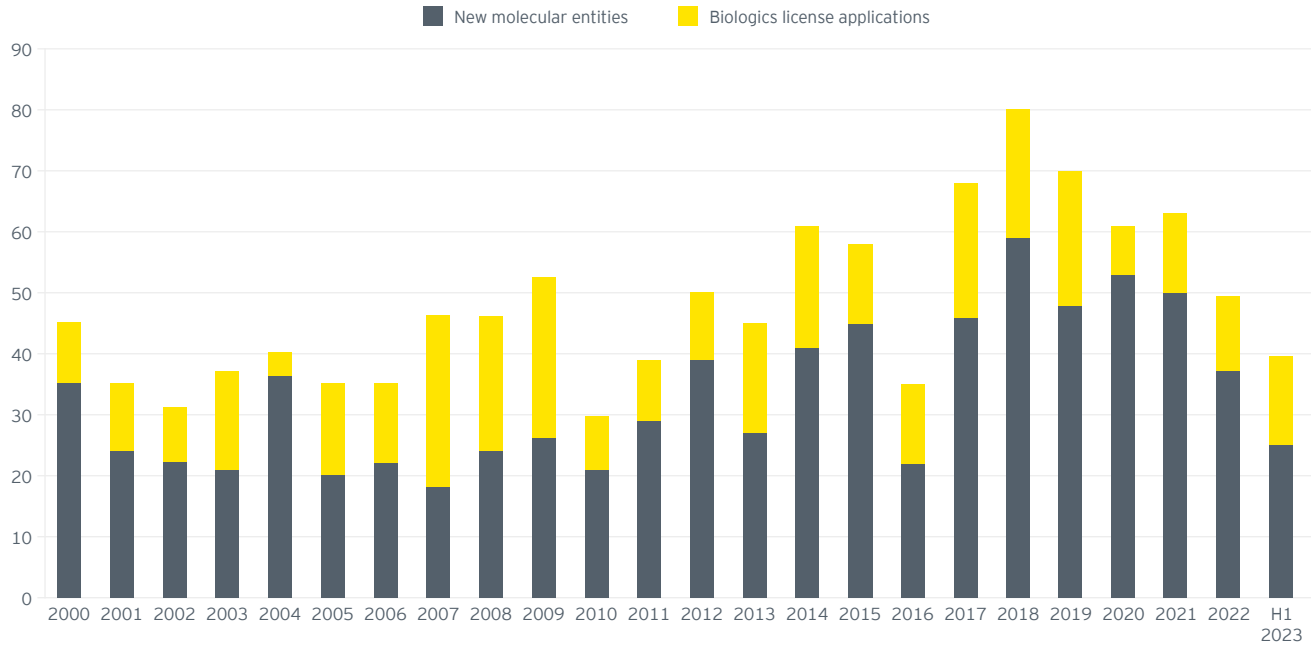
# A story of scientific resilience

## 37 NMEs
## 12 BLAs

FDA approvals for biotech in 2022

The biotech sector has enjoyed notable success in developing and launching new products in recent years, with an annual average of 69 US FDA approvals for new molecular entities (NMEs) and biologics license applications (BLAs) over the five-year period from 2017 to 2021. In 2022, the number of FDA approvals across all geographies dropped to 49 (37 NMEs and 12 BLAs; see Figure 7). Reportedly, the dip in approvals was primarily driven by staffing shortages at the FDA, which was seeking to fill over 400 jobs in 2021. As of H1 2023, the number of advertised roles had dropped to nearly 44,[7] encouraging hopes that the agency's approval and other regulatory processes will regain the momentum they lost during the pandemic crisis.

**Figure 7. FDA product approvals, 2000–H1 2023**




Sources: EY analysis, FDA website.
*Data for biologic license applications from 2000 through 2022; new molecular entities from 2011 through 2022
Note: For 2000 to 2011, NMEs include new biologics but exclude new indications, new formulations and generic drugs

7. *USAJOBS website*, https://www.usajobs.gov/Search/Results?a=HE36&p=1, 31 August 2023.

Despite the financial headwinds of the past 18 months, Texas biotech companies saw momentum in 2023 with new product approvals. In the initial six months of 2023, Texas saw the authorization of a total of three products, including two NMEs – Skyclarys from Reata Pharmaceuticals, mentioned above, and Inpefa from Lexicon Pharmaceuticals – and one BLA – Source Plasma for further manufacturing of injectable products from Join Parachute, LLC.

**Figure 8: Details of Texas specific FDA product approvals**

| Drug name | Approval date | Year | Name of company | FDA-approval use on approval date |
|---|---|---|---|---|
| Skyclarys | 28-02-2023 | 2023 | $150 | 2023 |
| Inpefa | 26-05-2023 | 2023 | $50 | 2022 |
| Detectnet | 03-05-2020 | 2020 | $40 | 2022 |
| Xermelo | 28-02-2017 | 2017 | $15 | 2022 |

Sources: EY analysis, FDA website.

As disruption continues for the biotech sector in Texas, we anticipate that several of the state's biotechs will face operational headwinds in the coming months, with 75% of the emerging biotechs we track in Texas having less than two years of cash on hand. However, even amid these tough financial times, companies that can shift to leaner operations and focus on financial resilience are likely to thrive. As such, we believe that the overall outlook in Texas, which remains a major US hub for biotech, represents a marked improvement over last year, infusing a much-needed sense of optimism into this dynamic sector defined by resiliency and data-driven diligence.

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