





Annual Biotech Report

We wish to connect private investors with emerging technologies that address global health challenges. To do so, first we must bring our investors closer to the biotech world.

Meet the LifeLink Team

LifeLink's most valuable asset are the talented and gritty minds of our team. In this edition of our annual report, we ask them to share a little more about themselves:

"Describe what scientific discoveries have inspired you in 2023?"

"What is your go to activity when you need to clear your head of company related business?"

Andrew MacRae

Associate at LifeLink Ventures in



"I'm fascinated by the resurgence of small molecules and how many new potential therapeutic mechanisms are being explored, from targeted degradation, to covalency, proximity induction and molecules targeting RNA. Seeing how these new mechanisms play out to traditional protein inhibition will certainly be exciting!"

"For the last decade CrossFit has been super important to me. I love being able to go the gym and know all I have to think about for the next hour is lifting weights and moving my body."

Investment analyst at LifeLink Ventures in

Ana Gallego



"Getting away from the city and immersing myself in nature is my ultimate relaxation. I'm a big fan of outdoor sports, from hiking to diving. In my day-to-day life, my go-to routines like yoga and CrossFit help me disconnect, but enjoying time with my loved ones is essential."



Pablo Heredia



Investment analyst at LifeLink Ventures in

"In 2023, I have been thrilled by AI's transformative role in drug development. The massive advancements in generative AI will not only allow us to predict a drug's behaviour before clinical trials but also reduce the time spent on drug development compared to just five years ago. This isn't just faster science; it's smarter, cheaper, and a big win for everyone looking forward to new treatments."

"To unwind from work, I love diving into a good travel novel or exploring the hidden gems of Barcelona. But what really does wonders to clear my mind is grabbing dinner with friends or hitting the court for a game of padel."

Meet the Founders

LifeLink Ventures is proud to have backed a group of dynamic entrepreneurs we believe are shaping the future of biomedicine. To glimpse into the driving forces behind these leaders we asked three portfolio CEOs two questions about work and life:

"Describe a recent scientific achievement that excites you going into 2024?"

"What is your go to activity when you need to clear your head of company related business?"

Amanda Wagner

CEO of Immunitas Therapeutics in





"When our VP of Clinical called me to tell me that we had a patient with substantial tumour shrinkage, who was being only treated with our drug. That moment was huge".

"A couple years ago I started doing 5-8 minutes guided meditations, layered on top of running and hot yoga. It's helped me step away from work and be more present in other moments of life (like dinner with my kids!)."

ochrebi

CEO of Ochre Bio in

Jack O'Meara

"Seeing early signal of one of our leads impacting key parameters of liver health during machine perfusion was pretty inspiring. Another was the selective delivery of a cancer killing agent to liver cancer cells in vivo - a pretty exciting validation of an early hypothesis we had had for hepatocellular carcinoma (HCC). Scientifically, been an exciting year at Ochre."

"I am addicted to Barry's Bootcamp. The brutality of an hour sprinting, pumping weights, and jumping around (while someone shouts positive affirmations at you) is quite a powerful way to clear the head."



Stephen Myatt

CEO of Macomics in

macomics



"This year marked a significant achievement for our ENIGMAC discovery platform by completing what we believed was the first large-scale gene editing screen in human macrophages. We look forward to its exciting applications in oncology and other disease areas, fostering portfolio expansion and collaborations for novel therapeutic discovery".

"I am lucky to live near the countryside in the UK and enjoy walking in the local hills in my spare time. It is a wild and often wet and windy landscape, but the worse the weather the better for clearing the head. I am also often to be found at the local climbing wall, although these days I tend to have little time to climb, instead spending the time belaying my children!"

2023 Annual Biotech Report

Highlights

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	NVIDIA enters the biotech market
3.	Inflation Reduction Act – New Incentives
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1. Biotech in 2023

Public Markets

Biotech stocks have underperformed since their peak in early 2021, as seen by the downward spiral of the XBI index fund through mid 2022, while stocks have remained stagnant in H2 of 2023. Markets have been harsh even to those with strong cash positions, as an estimated 200+ life science companies were trading below cash as of Oct 2023¹. However, **the hope for US federal interest rate cuts in 2024 suggests a potential rebound in the coming 6 to 12 months**.



Public Offerings

Biotech IPOs in 2023 were down from 2021 highs, with a total of 2 billion raised compared to 32 billion USD, respectively. Stocks for companies that went public in 2023 are overall performing down, with an average change in stock price of -20% since initially listing. Notably this includes Structure Therapeutics, a company that is up 50% (market cap >\$1.5B), likely as a result of its participation in the development of orally available obesity drugs.

Number and value raised in biotech IPOs



Mergers & Acquisitions

Despite challenges posed by public markets, M&As saw a boost in spend (141 billion USD), as pharmas continued to source new products from biotech. Expenditure doubled from 2021 or 2022 even though total number of 2023 acquisitions decreased. **Trends include the preferential purchase of clinical and commercial stage companies targeting large markets**. Examples include Pfizer's mega acquisition of oncology company Seagen (founded in 1997) for 43 billion USD and Roche's acquisition of obesity company Carmot (founded in 2008) for 2 billion USD.

Number and value raised in biotech M&As



Interpretations

S While public markets suggest biotech is underperforming, M&A suggests a healthy landscape of innovation. Assuming COVID overvalued the market and that since then rapidly raising US interest rates overcorrected that value, **it is possible that interest rate cuts in 2024 drive the market towards a more sustained positive growth**.

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2. Opportunities in Artificial Intelligence

NVIDIA and AI Drug Development **Artificial intelligence** continues to be leveraged by the biotech sector and benefiting those with high quality data sets that are otherwise too large and complex from which to extract biological learnings. Such data sets include patient genetics and high throughput drug screenings.



In 2023, chip maker NVIDIA emerged both as partner and investor to the biotech

industry, initiating multiple collaborations including ones with Genentech and Recursion. Both collaborations partially serve to accelerate NVIDIA developed generative AI models for drug discovery. Referred to as the BioNeMo platform, NVIDIA will use partner data to refine the model, advance partner drug pipelines and sell access to a commercial version of the software.

Since inception, LifeLink portfolio company, Ochre Bio, has employed AI to develop precision RNA medicines for liver disease. Their strategy includes generating a detailed atlas of genetic data from patients with chronic liver disease. The company has integrated AI models to identify and test new drug targets while deciphering disease mechanisms at a molecular level.

3. U.S. Inflation Reduction Act

New Incentive Structures

In 2022, U.S. President Joe Biden executed a package of federal laws aimed at reducing inflation. The package included legislation providing Medicare with the ability to negotiate drug prices **aiming to lower the price of certain therapies** (10 nominated drugs per year). While the act is projected to save billions in spending, aspects of the laws, its restrictions and the negotiation timelines are expected to create different incentive structures for biotech and pharmaceutical companies. Examples include:

1. Since rare disease drugs (often called orphan drugs) are exempt from negotiations when approved for only one disease, there will less incentive to expand approved orphan drugs to other diseases where patients could also benefit².

 Due to the negotiation timelines disfavoring small molecules, there is a financial incentive to develop antibody-based therapies instead, which may negatively impact patients with diseases better addressed by small molecules³.

After expressing concerns that these incentives could negatively affect innovation, patients and profit margins, multiple pharmas have initiated legal actions and claim the act violates the US constitution. However, it remains to be fully determined how the IRA will impact on the pharmaceutical and venture industry.

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4. LifeLink Areas of Interest

Oncology

In the second quarter of 2023, the FDA and the EMA have approved more than 21 new oncology agents, including multiple expansions of previously approved agents into new cancer types⁴. Despite this progress, from a commercial perspective, clinical oncologists have disproportionately relied on a limited number of therapies and targets. Statistics include the fact that over 40% of all solid tumor approvals from 2017 to 2021 target one pathway (PD1⁵) and that the top 5 clinical oncology targets have dozens of companies developing assets against the same targets⁶. While oncology is a highly competitive market, it does represent a substantial portion of mergers and acquisitions as most large pharmas maintain oncology pipelines².

LifeLink remains dedicated to oncology with a strategy of prioritizing differentiated

therapies that leverage novel targets, nontraditional cell types and that are developmentally guided by patient data, as represented by portfolio companies Immunitas, Macomics and InCephalo.

Neurodegeneration

In 2022, the Alzheimer's therapy landscape was shaken by the launch of a much-anticipated drug, Aducanumab, which ultimately fell short commercially (achieving only \$4.8 million in sales compared to the initial \$12 billion projection from Goldman Sachs analysts). Challenges included the necessity for initial and subsequent MRI scans — a costly and not universally accessible equipment — and the emergence of concerning side effects such as cerebral oedema and microhemorrhages, complicating treatment continuity.

Hope continues into 2023, with Biogen's Alzheimer's drug Lecanemab showing stronger clinical data. Biogen will shift towards assessing broad effects on slowing cognitive decline. Additional positive results from a late stage clinical trial sponsored by Eli Lilly⁸, will create direct market competition for Biogen, as both companies compete to demonstrate superior cognitive protection in Alzheimer's patients. **These developments are a culmination of decades of scientific research and suggest neurodegeneration can finally be treated in a manner that slows down – and perhaps in the future halts – cognition decline in these diseases.**



5. 2023 Stories

Advances in Inflammation

Engineering patients' immune cells to drive an anti-cancer response has emerged as a therapy capable of curing certain blood cancers (such as certain leukemias). Successes have energized the field to apply cell engineering to diseases outside cancer. In the context of auto-immune and inflammatory diseases, immune cells can be engineered to eliminate populations of pathogenic over-activated immune cells.



In November 2023, a study at the University Hospital Erlangen (Germany) reported updated results for 15 patients treated with engineered T cells designed to eliminate B cells that induce autoimmune complications associated with lupus, systemic sclerosis, and inflammatory myositis^a. **Over two years into the study, multiple patients remain in remission without the need for additional standard of care drugs.**

Genome Editing

2023 marked a significant milestone in the field of genome editing with the approval of the world's first CRISPR based gene editing therapeutic, CASGEVY, by Vertex Pharmaceuticals and CRISPR Therapeutics. This groundbreaking development offers a new therapeutic avenue for patients with sickle cell disease and highlights the remarkable speed at which CRISPR genome editing technology went from academic breakthrough to Nobel Prize awarded and to commercial therapeutic in just over one decade.

CASGEVY is unique in that, rather than rewriting the underlying genetic mutation of sickle cell patients, it employs CRISPR technology to edit the genome of patient blood cells and reactivate the expression of a fetal version of hemoglobin, countering the pathogenic effects of mutated hemoglobin present in these patients. Nonetheless, while the therapeutic has proven effective, its administration requires immense patient dedication:



- Stem Cell Collection Hematopoietic stem cells are harvested from the patient's bone marrow or peripheral blood.
- CRISPR-Cas9 Gene Editing These cells are then edited in the lab using CRISPR-Cas9 technology to increase fetal hemoglobin production.
- 3. Chemotherapy Before reinfusion, patients undergo chemotherapy to deplete their existing bone marrow, making space for the edited cells. Since chemotherapy can compromise fertility, many patients will choose to collect eggs or sperm prior. In the U.S., the egg preservation process may cost about \$20k.
- Cell Transplantation The genetically modified stem cells are infused back into the patient.

6. GLP-1 medications and obesity

What is GLP-1 medication and for what is it used? Since first approved in 2005, GLP-1 medications (which mimic a natural hormone that responds to nutrients in the gut), have been crucial in **treating obese Type 2 diabetes (T2D) patients.** These drugs act **by enhancing insulin secretion, inhibiting glucagon secretion**, and **impacting digestion** by slowing intestinal movements. All these effects contribute to a control of sugar in the blood and result in weight loss in these patients.

Side Effects Despite its unquestionable success, GLP-1 medications could pose real risks, including renal impairment, pancreatitis[™], and thyroid cancer 1-3 years after treatment[™], along with mild but common side effects like vomiting, nausea, and diarrhea[™]. Furthermore, it is noteworthy that using these drugs without medical supervision and lifestyle changes may result in two-thirds weight regain upon discontinuation[™] and they are recommended for patients with obesity (BMI≥30) or overweight (BMI≥27) with concurrent conditions like diabetes, hypertension and sleep-related respiratory issues, among others. The impact on healthy individuals without these characteristics remains unstudied.

Market GLP-1 medications have sparked the interest of major pharmaceutical companies which is reflected in cases such as the \$2.7B acquisition of a biotech company specialized in GLP-1 by Roche¹⁴ and license agreements from AstraZeneca¹⁵ and Sanofi¹⁶. Demand for Ozempic, Wegovy and a similar Lilly drug, Mounjaro, has skyrocketed over the past year¹⁷. ¹⁸ with the expected obesity drug market size reaching \$77 Billion by 2030¹⁹. **GLP-1 medications are now within the top three highest selling drugs.**

Indication	Dosing Frequency	Administration route	Drug
	Twice daily	Subcutaneous Injection	
Diabetes	Once daily	Subcutaneous Injection	JAdlyxin° ViCTOZA°
Diabetes		Oral	RYBELSUS [°]
	Once weekly	Subcutaneous Injection	trulicity. Ozewert mounjaro
Obesity	Once daily	Subcutaneous Injection	Saxenda
Obesity	Once weekly	Subcutaneous Injection	wegovy zepbound»

*All drugs mimic GLP-1, with Mounjaro and Zepbound from Eli Lilly additionally mimicking GIP hormone.

New Efforts

In ongoing clinical trials, Eli Lilly is testing a new GLP-1 drug, retatrutide (nicknamed "triple G"), that also mimics the GIP and glucagon hormones, aiming to help patients lose up to 24% of body weight (compared to 15% reported for Ozempic and 20% for Mounjaro)²⁰. Recent studies also showcase the role of GLP-1 in preventing cardiovascular problems²¹ and improving fatty liver disease²². But the future of GLP-1 medications could expand even further: ongoing studies are exploring its potential in treating alcohol and tobacco addiction by acting on brain reward circuits associated with motivation and intake²³.

7. Contact

For more information on LifeLink Ventures or our portfolio companies please reach out or visit our webpage:

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