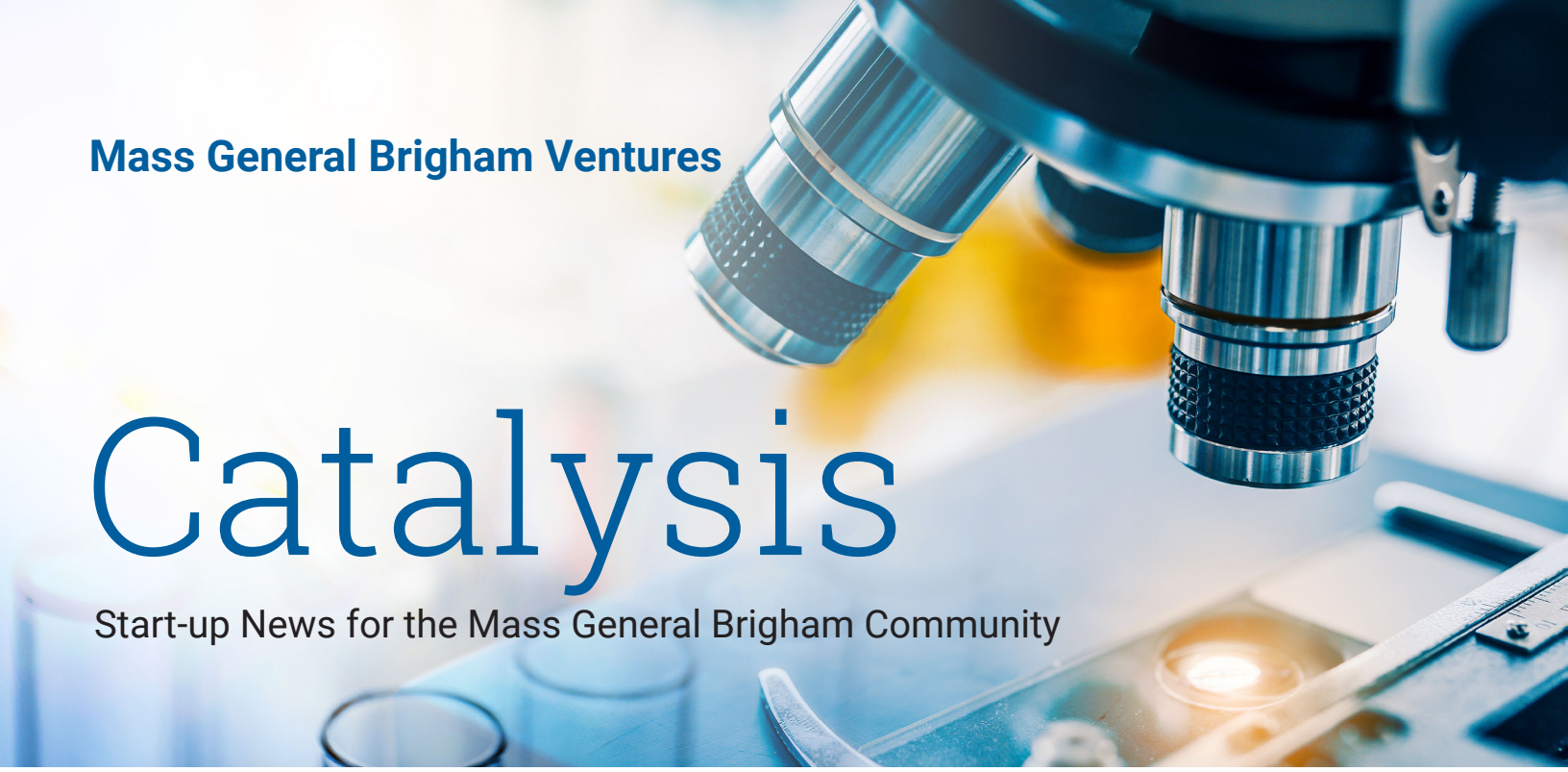

Mass General Brigham Ventures

Catalysis

Start-up News for the Mass General Brigham Community

Our Spotlight on Amolyt, Mediar and Violet

In this issue, we highlight three companies: Amolyt, Mediar, and Violet. All three were created, in part, by **Meredith Fisher, PhD**, a partner at Mass General Brigham Ventures (MGBV). These companies required a mix of entrepreneurship and science to grow, and we highlight them to underscore how MGBV works with the community and to accentuate how the founders and entrepreneurs built these great companies. Each company required a compelling collaborative effort to get its company off the ground.

Amolyt required fluency on both the part of the company and the founders–in particular, trust from the PIs that their hard work and intellectual insights in endocrinology would be appreciated and invested in wisely. It also required the company to work without a trace of "not-invented-here" attitude, a willingness to bridge the gap in academia, and to make it clear that they cared deeply about the professor's hard-won insights.

For Mediar, it required three investigators all willing to pool their ideas into a single company, and a CSO who made certain that thorough and equitable attention would be provided to each of their fibrosis efforts.

For Violet, it helped tremendously that the principal investigator trusted that MGBV could build the company, and that the PI's and other founders' professional insights would be developed in the seed stage and beyond.

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For all three companies, personal commitment, laying aside egos, and collaborative focus were essential to nurturing the translational efforts.

We look forward to seeing how these companies develop further. While they're all at different stages, with Amolyt in late-stage clinical trials, Mediar getting ready to enter the clinic, and Violet getting started with drug discovery, the essential piece of their development remains the same. Relationships between scientific founders, company executives, and investors remain paramount (perhaps a note to remember in this "age of AI"). We hope to witness each deliver great medicines for patients in endocrinology, fibrosis, and neurodegeneration.

— Roger Kitterman

Mass General Brigham

Amolyt Pharma – Lead Molecule Has Longer Half-Life for Better Outcomes in Endocrinology

Amolyt Pharma is a clinical stage company focused on rare endocrine disorders. It was founded by CEO Thierry Abribat, PhD and CSO Michael Culler, PhD, who had been collaborators on and off for decades, often discussing starting a new company. Thierry had previously started two single-asset companies: Alizé Pharma, acquired by Millendo Therapeutics, and Alizé Pharma II, acquired by Jazz Pharmaceuticals. For his third company, he wanted a robust pipeline with multiple assets to diversify and de-risk the effort.

Mike is an endocrinologist with experience at NIH, J&J, and Ipsen. He and Meredith Fisher had connected via an introduction from **Anne Klibanski**, the CEO of Mass General Brigham. Meredith was impressed with Mike's background and experience at Ipsen with overseeing multiple programs through clinical proof of concept trials. When Meredith learned that there was an exciting endocrinology program developed by **Tom Gardella, PhD**, and others at MGH, which was becoming available for license, she reached out to Mike immediately. The effort focused on a long-acting parathyroid hormone receptor 1 agonist, later named Eneboparatide.

Thierry and Mike worked with Meredith and her colleagues to in-license the program and then continued to work with MGBV to develop the program. They renamed the company, originally called Alizé Pharma 3, to Amolyt after ammolite, a rare iridescent gemstone found within ammonites—fossils of a type of shelled cephalopod. The ammonite shell has a spiral shape, which they felt reflects the journey of a patient from disease toward recovery.

Since Amolyt's founding in 2018, it has raised $75 million in a Series A (one of the largest venture-led Series A financings in Europe), $80 million in a Series B, and $138 million in a Series C financing. Amolyt has brought Eneboparatide into Phase 3 trials and acquired two other assets.

Eneboparatide is a parathyroid hormone receptor 1 agonist originally designed to treat hypoparathyroidism, a rare disease caused by damage to or removal of the parathyroid gland, which results in low levels of parathyroid hormone. The condition causes low calcium levels, muscle cramps and spasms, bone loss, and in severe cases can cause seizures, irregularities in normal heartbeat, and spasms in the airways, possibly leading to respiratory failure.

Hypoparathyroidism is usually treated with supplemental calcium and vitamin D, but these supplements can cause kidney stones and chronic kidney disease due to the excess calcium. Treatment with native parathyroid hormone is ineffective because the hormone is flushed from the body within two hours due to its short half-life. Eneboparatide acts in a similar manner to parathyroid hormone but remains active for significantly longer by remaining attached to the receptor. It maintains calcium in a normal range, while also stimulating active reabsorption by the kidneys, thereby protecting bone tissue.

> "It has been a privilege to watch the Amolyt team advance eneboparatide, originating from Mass General Brigham through initial clinical PoC, and now initiating the Phase 3 registrational trial within four years of their first financing," notes Meredith. "Hypoparathyroidism currently has no available approved therapeutics, and we are hopeful that if approved, eneboparatide will produce a much needed treatment for these patients."

Amolyt's other programs also address endocrine diseases. ACP-3813, a cyclic peptide growth hormone antagonist, was licensed from the Japanese drug development company PeptiDream and is under development for acromegaly, a condition where the pituitary gland produces too much human growth hormone. The therapeutic is currently in GMP tox studies. Another program targets monoclonal antibodies against parathyroid receptor 1 for primary hyperparathyroidism and humoral hypercalcemia of malignancy.

The company continues to look for external opportunities in the rare endocrine and related disease space, diversifying its pipeline to ensure continued success and to find solutions for those suffering from these rare diseases. It is hoped that MGB can provide further support with some of the programs in its portfolio.

Mediar Therapeutics – A Focus on Fibrotic Mediators

Mediar Therapeutics focuses on fibrosis progression, utilizing an innovative approach that halts disease by targeting fibrotic mediators that can be measured in blood and correlate with disease severity. Unusually, Mediar originated from a combination of three separate fibrosis programs from three different researchers at MGH and BWH, who were identified by Meredith Fisher.

The three principal investigators were unaware that they were working on similar programs in the same hospital system, using the same novel approach— assessing the pathological role of the myofibroblast in fibrosis and its role in build-up of the extracellular matrix. When approached by Meredith, the three understood that there would be greater strength in pursuing their efforts within one company.

Fibrosis is caused by internal injury or inflammation, which leads to the thickening and scarring of tissues. This thickening interferes with normal organ function and is a compounding factor in many common ailments, including heart, lung, liver, and kidney diseases. Fibrosis itself leads to approximately 45% of deaths in the industrialized world. Few treatments for fibrosis exist, and those that do have limited ability to delay or reverse disease progression. Mediar is pursuing fibrotic mediators that play a role in converting the quiescent tissue fibroblasts (cells that contribute to the formation of connective tissue) into pathological myofibroblasts or scar-forming cells. By blocking fibrotic mediators, the progression of fibrosis can be arrested and potentially reversed.

With the guidance and insight from the scientific founders, Meredith led the seed financing of the company and ultimately raised $20M from investors, including Mission Bio Capital, Ono Ventures, and Pfizer Ventures. Meredith stayed on as interim CEO and was able to recruit Paul Yaworsky, PhD, who joined as CSO and the first employee post-financing. Paul's arrival at Mediar enabled the three nascent monoclonal antibody discovery programs to take off. Prior to Mediar, Paul was COO of Inflammation & Immunology Research at Pfizer, where he developed the scientific and business plan for fibrosis research and led the fibrosis team.

The Mediar team further expanded ahead of its Series A, recruiting Simon Sturge as Executive Chair. They then raised an $85M Series A round led by Novartis Venture Fund and Sofinnova Partners and recruited Rahul Ballal as CEO and Jeffrey Bornstein as CMO. The team has built out its research and clinical capabilities and just passed the 30 employee mark this fall.

> "I'm thrilled that for Mediar we could take advantage of our proprietary access to new biological paradigms from researchers at the hospital, which represent truly novel approaches for therapeutic intervention. Fibrotic diseases are a huge unmet need; yet venture has historically under-invested here," said Meredith. "The opportunity to enable a company leveraging novel insights in disease biology from Mass General Brigham research is extraordinary, and we are very happy to see other top tier investors and pharma companies join us on this journey."

Mediar has advanced two lead programs to clinical candidate stage with hopes to initiate clinical studies in 2024. The first program, MTX-463, is an antibody that targets WISP1, a matricellular protein shown to play a role in the conversion and persistence of the fibroblast to myofibroblast transition. The company's second program, MTX-474, is a first-in-class monoclonal antibody designed to neutralize the EphrinB2 signaling that causes the progression of fibrosis and may play role in defining the fibrotic niche. Both candidates have the potential to target multiple indications, including fibrosis affecting the lung and liver. Preclinical *in vivo* and *ex vivo* studies have demonstrated the effectiveness of both efforts.

The third program promotes extracellular matrix assembly, cell adhesion, and fibrosis. Mediar is optimizing antibodies and generating the data to support clinical candidate nomination. The target is upregulated in end-stage kidney disease and has more recently shown to be highly induced in stage 4 non-alcoholic steatohepatitis.

The collection of assets that Meredith and Mediar uncovered enabled recruitment of top-notch talent and helped to position Mediar as a leader in anti-fibrotic drug discovery. As they progress towards clinical trials, we eagerly await results from Mediar to see how they help patients suffering from various fibrotic diseases.

Violet Therapeutics – A First-In-Class Platform to Map and Drug the Cellular Connectome

Violet Therapeutics emerged from stealth mode in May 2023 with the announcement of $10.6 million in funding. The round was led by Dementia Discovery Fund and the University of Tokyo Edge Capital Partners with Ono Ventures joining MGBV, the founding venture investor.

Violet is a therapeutics company leveraging CONNECT, a proprietary platform for the identification of cell-cell interactions with a specific focus on diseases of the central nervous system (CNS). Cell-cell interactions are known to control the physiology and pathology of the CNS as well as other organ systems and these interactions can be exploited for therapeutic development. By mapping the cellular connectome at scale, Violet can identify and validate novel targets which are not driven by genetic mutations to build its pipeline of new therapies. The CONNECT platform technology was originally developed by Violet's founder, **Francisco Quintana,PhD**, Professor of Neurology at Brigham and Women's Hospital and Harvard Medical School.

Meredith Fisher, PhD, a partner at MGBV and original CEO of Violet, along with co-founder Dr. Quintana collaborated to create the company, just as the publication of the foundational paper in Science was published in 2021. Meredith and Fran had been working together for several years as Fran developed the initial platform and this allowed Violet to emerge in lockstep with the scientific progress from the Quintana Lab. They both saw the differentiation of the technology and the potential for it to become a first-in-class discovery platform.

At scale, the CONNECT platform can identify and map thousands (or even millions) of cell-cell interactions that underlie normal physiology and disease pathology. Additionally, the Quintana Lab, along with collaborator and co-founder **Kevin Hodgetts, PhD**, Director of MedChem and head of Laboratory for Discovery in Neuroscience at BWH, identified and advanced a small molecule program against the first validated and novel neuroinflammatory therapeutic target to emerge from CONNECT: EphB3. EphB3 is a receptor tyrosine kinase that was identified by the CONNECT platform and is involved in axon guidance and mediates microglia-astrocyte interactions. While EphB3 had been previously described in developmental aspects of CNS function, it was not until the full interactome of a neuroinflammatory cascade was identified by the CONNECT platform that the target was recognized for its role in neuroinflammation pathology.

The initial funding from MGBV, and more recently an expanded syndicate, has enabled Violet to grow its operations and team. While Meredith remains as interim CEO, Violet has recently recruited Darby Schmidt to be its Chief Scientific Officer. Darby is a medicinal chemist by training and prior to Violet has had an impressive career in early-stage biotech companies, including Caraway and Quartet, an MGBV portfolio company. As Violet was looking to expand its team post financing, Meredith and Darby met and saw the potential for Violet to advance their lead program (EphB3) and first-in-class discovery platform.

"I have been involved in several early-stage startups and have seen them grow and develop, so I was struck by Violet's unique position," said Darby. "Violet has a great founding team, complemented by an advanced program and a well-developed platform. Biology is entering the era of big data, and Violet is an opportunity to engage while there is still so much to explore," she said.

"When I was introduced to the Violet platform: CONNECT, I saw that it has the power to be a 'missing link' in understanding big biology data. In addition, we have a unique and advanced small molecule program identified by the platform that can rapidly advance to the clinic for the treatment of neurodegenerative diseases such as ALS, Alzheimer's Disease and frontotemporal dementia, where we have limited treatments for patients and a significant need for new targets to treat these indications."

Looking toward 2024, Violet is focused on advancing its lead program through in vivo proof-of-concept and continued expansion of the CONNECT platform to a broader set of indications and pathologies beyond the CNS. As Meredith notes, "we are uniquely positioned at Violet to exploit the scaled biology our CONNECT platform enables to find and prosecute novel, interactome-based targets across multiple indications while also focusing on advancing our internal pipeline to develop new therapies in the form of small molecule programs that current technologies can neither identify nor drug without the unique capabilities of CONNECT."

Funding updates

Mass General Brigham Ventures plays a critical role in founding and funding next-generation technologies. Since inception in 2008, we have invested over $200 million in 57 venture startups. The current portfolio includes a number of transformational companies focused on CNS/ neurological disorders, immunology, and gene and cell therapy.

During 2023, MGBV continued to strategically deploy capital to reinforce our portfolio companies' efforts, enabling them to pursue critical milestones, accelerate research and development, and advance toward transformative clinical outcomes. Notable financings included a $155 million oversubscribed Series B round for **Abcuro, Inc.** in August (more), an $88 million Series B extension for **QurAlis Corp.** (more), and a $138 million (€130 million) Series C financing for **Amolyt Pharma**. Amolyt's Series C financing represented the largest European biotech investment round in the first half of 2023 (more). **Garuda Therapeutics**, launched with a $72 million Series A in Feb. 2021, and closed an additional $62 million Series B venture round in Feb. 2023. Garuda is a cell therapy company developing off-the-shelf hematopoietic stem cells (HSCs) to treat a broad range of severe and life-threatening diseases.

Key Statistics

$450M
Capital Under Management

- 57 Portfolio Companies
- 16 Exits
- $140 M Realized and Publicly Traded

Clinical update

Mass General Brigham Ventures portfolio currently has 19 clinical stage companies with 36 ongoing trials – comparable to a medium-sized biopharma company.

The successful clinical development underscores the collective effort of Mass General Brigham's extensive ecosystem to address unmet medical needs. Notable events in 2023 include **Amolyt Pharma's** initiation of a Phase 3 Clinical Trial of eneboparatide (AZP-3601) for the treatment of hypoparathyroidism (more), **Abcuro's** Phase 2/3 Study of ABC008 for the Treatment of Inclusion Body Myositis (more), and the advancement of **Swan Bio's** first-in-human study of gene therapy for adrenomyeloneuropathy (AMN) to a higher-dose cohort (more).

These developments demonstrate the important role of venture capital in advancing medical science and highlight the successful efforts of Mass General Brigham to apply both financial and human capital to advance cutting edge technologies. This approach is vital for addressing unmet medical needs, advancing the medical field, and ultimately improving the quality of healthcare for patients.

19
clinical stage companies

36
ongoing trials

Phase I	Phase II	Phase III
18	10	8

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