

Catalysis

Start-up News for the Mass General Brigham Community

Reintroducing Catalysis

We're back with the newsletter after a lengthy hiatus for the pandemic to bring you updates from Mass General Brigham Ventures (MGBV).

For this newsletter, we felt it appropriate, given the nature of the last couple of years, to start with two mental health efforts, InStride and Rippl Care. InStride focuses on adolescents, primarily on the treatment of anxiety and OCD, and Rippl focuses on seniors, specifically those with Alzheimer's and related dementias. Both new companies have roots in McLean Hospital, given the fount of mental health expertise at McLean that gives us great pride to be doing our part to help offer these programs to patients.

There are several themes common to both efforts, despite the obvious difference in terms of patients (e.g., adolescents vs. seniors). These themes involve starting locally (whether that's in Boston for InStride or Seattle for Rippl) with plans to expand nationally while ensuring that quality is maintained as the business grows. Both companies approach patient treatment holistically, integrating support, education and communication with caregivers, family and other service providers in their programs. And, since they are businesses, they also consider the payer perspective, which is clearly critical for a sustainable business, especially in the field of mental health where the majority of care is not covered. The ability to provide treatment virtually is a great help on that front because computer-based care allows for technological insights and applications to be tailored to treatment and caregiving, knitting together the disparate voices that can make care so challenging for family members managing at the front lines. Since the companies are deeply connected with Mass General Brigham, evidence-based treatments are also a theme,

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leveraging what has been learned through hospital practice. Both companies have strong ties to our faculty who ensure that hospital insights are truly incorporated into care plans.

The companies have health equity as a core part of their mission, making sure the treatments are affordable and available to everyone who needs them, regardless of financial situation or geographic location. In Rippl's case, they are also hoping to reduce the cost of care through reduction in emergency room visits by providing sustainable, routine, preventative care. This should help hospitals to function more effectively, improving outcomes for patients with Alzheimer's and related dementias while also easing our overburdened hospital systems.

There are elements of academia, technology, business and entrepreneurship running through each company. We very much hope that they are successful entrepreneurial businesses, and that they're able to take the best aspects of McLean care for these patient populations and, combined with modern technology, start to build back the foundation of mental health that's been so under duress over the last few years.

We hope you enjoy these founding stories.

— Roger Kitterman

InStride Health's virtual care model delivers needed mental health care to children and adolescents

Mental health practitioners Mona Potter, M.D., and Kat Boger, Ph.D., met on McLean Hospital's unit for children and adolescents struggling with co-occurring substance use disorders and mental health issues. Children there were being treated for substance use, but they were also facing anxiety that was undiagnosed, untreated, and not properly managed. Once the treatment ended, there wasn't specialty follow-up care. To manage the needed follow-up care, Potter and Boger co-founded the McLean Anxiety Mastery Program with Jacqueline Sperling, Ph.D., focusing on children and adolescents burdened with anxiety and OCD.

"Historically children with anxiety and OCD would be grouped with other mental health disabilities which meant they weren't getting treatments targeted towards their specific needs. By specifically addressing their needs, we were getting incredible outcomes" says Potter.

While Potter and Boger found success, they were only scratching the surface of the problem. "There's a dearth of treatment in general," Boger says, "but also evidence-based treatment specifically. These kids are really struggling; their lives have fallen off track, they are no longer engaging in the things they care about because of their anxiety and OCD. Yet only children in families that live near academic medical centers and have the financial means are able to access evidence-based treatment."

Families desperate for solutions were moving to Boston from all over the world to enroll in the McLean program, often spending money beyond their means. "We've seen families who've depleted all their resources just trying to get the right care, literally cashing in college funds," says Boger. Families unable to afford relocation or treatments are left without access to appropriate care.

The drive to make this type of treatment more accessible led the clinicians to create InStride, with InStride's founding CEO John Voith and CTO James McElhiney, with the mission of providing desperately needed access to evidence-based, insurance-based care for children, teens, and young adults with moderate to severe anxiety and OCD.

"During COVID, so many families I knew had children who were experiencing anxiety, it became something I was personally interested in. At the same time, the flood of media coverage highlighted the public health emergency resulting from an intense shortage of appropriate mental



Mona Potter, MD
Chief Medical Officer and
Co-Founder



Kathryn Boger, PhD ABPP
Chief Clinical Officer and
Co-Founder

health treatment for kids and teens," Voith says. "I met Mona, Kat and James, and we had this great balance of shared mission and diverse skill sets so I felt we could really make this happen."

In addition to the strength of the leadership team, Voith found that InStride's partnership with investor groups was a real strength in both launching InStride and expanding it. "We have a fantastic group of supportive investors, including MGB Venture, 406 Ventures and now Valtruis, who bring deep experience and expertise in digital health and value-based care to the table. This is a tough problem to solve, so having a diverse range of experience and expertise is critical."

Potter and Boger found that the pandemic dramatically exacerbated the incidence of anxiety in adolescent populations, but also provided proof of concept for the effectiveness of telehealth as mental health care largely went virtual. They discovered additional benefits of virtual care, including improved accessibility and greater flexibility in health care delivery.

Traditional mental health services are often insufficient, particularly for youth with moderate to severe symptoms. Virtual care enables the patient to interact in their everyday environment. They can put on headphones and use a portable device in their community when they're

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in session with their therapists. It’s a lively and engaging treatment that helps generalize the learning to real life.

InStride also differs from traditional care by offering multiple touchpoints throughout the week, including group and coaching sessions at a frequency to match the patient’s needs. Team members are on call 24/7 so that a patient can access assistance during stressful episodes. They also incorporate the family into the care process in multiple ways, including family meetings and weekly groups where parents and caregivers are trained in strategies to most effectively support their child in managing their anxiety and OCD. “Parent and caregiver groups equip family members with skills and help them feel like somebody is on their side,” Boger says. “This can be a really isolating and lonely experience. You can feel like you’re the only parent whose child is struggling.”

Engaging families is particularly important because caring for a child who has anxiety and OCD is often counterintuitive, says Boger. Every instinct is to protect kids from the things that are hard, and being part of a treatment program helps families feel like they have a road map.

Accessibility guides every part of InStride’s program, from simplifying enrollment to collaborating with payers to promote awareness. InStride is fortunate to have great payer partners who recognize that this is a big problem, and that commitment to change is essential. As Potter says, “we’ve had this amazing experience of being able to consider the design of this program from the patient, family, clinician, and payer perspectives.”

While InStride began working with children, teens, and young adults in Massachusetts, the company has slowly expanded into neighboring states. They plan to be a 50-state solution, but they’re being deliberate and strategic about how they’re growing to avoid sacrificing quality.

One of the ways InStride ensures that the company maintains the quality and focus of the original program is through measurement-based care. “We have a very specific quantitative assessment,” Voith says, “that we use to examine all aspects of clinical quality, an analytical infrastructure that pushes daily reports to help us understand how we can stay on track and ensure that we’re meeting goals. This process provides very transparent feedback to team members and allows us to take corrective action when needed. So, we’ve defined quality in a very concrete way.” InStride brings the academic, business, and entrepreneurial worlds together, and as Potter says, “it’s a privilege to take care of these children and families, and we owe it to them to approach care thoughtfully and effectively”.

Rippl Care: Addressing behavioral health for seniors

An estimated 5.8 million Americans, 65 and older, are living with Alzheimer's disease and related dementia, but there's a startling lack of behavioral health care available to support them. Despite the increasing number of seniors with behavioral health issues, only 3% of psychiatric clinicians specialize in geriatrics. "We're only training 50 new geriatric psychiatrists per year in the U.S. We will never have enough clinicians trained to care for our aging population," says Dr. Brent Forester, formerly Chief of Geriatric Psychiatry at McLean Hospital, Associate Professor of Psychiatry at Harvard Medical School, and Scientific Advisor at Rippl Care. "And that's why I'm so excited about Rippl; it's scaling our expertise with teams of people, clinicians and non-clinicians, who can support seniors in the settings where they're already being cared for."

Why are there so few specialists? "Most of my colleagues in medicine don't even know we exist," Forester says. He explains that there are few opportunities for medical students to become aware of the specialty. On top of that, the Medicare reimbursement system makes it difficult for geriatric psychiatrists to afford to have private practices. "Most geriatric psychiatrists who do only private practice have to be really creative to make ends meet," Forester says.

Rippl Care is designed to address both these challenges: the lack of experts in geriatric psychiatry and the lack of available funding. Rippl is the brainchild of Kris Engskov, former President of Starbucks U.S. After he left Starbucks, he became involved in senior assisted living. "I'd always wanted to work in healthcare," he says. "I went to what I thought were the weakest points of healthcare, informed by my own experiences with my family."

Engskov was shocked by what he found there. "We were sending people to the ER because we couldn't manage their behavioral symptoms, despite the fact that we had a fair number of clinicians on staff." Confounded by the problem, Engskov started digging. "We had actuaries look at the 2019 claims data and found that people with dementia visited the ER three times more than any other chronic disease, and from there they were 75% more likely to be admitted to the hospital."

"It's a very traumatic experience," Engskov says. If a patient is delusional, a very common symptom of dementia, they may not be aware of why they're in the emergency room and once they have been admitted, they may be kept for several days for observation, often in facilities that are not designed to accommodate geriatric



patients with behavioral health problems. Geriatric psychiatric wards are uncommon, and even in hospitals with available wards there are often not enough beds. "They wind up on a general medicine floor where the staff often doesn't know how to manage these vulnerable patients. They put them in physical restraints and then the patient gets worse, not better. They're sitting in a bed for days at a time, not walking around. They get deconditioned and immobilized. There are medical complications and emotional trauma," Forester says.

It was this lack of behavioral health infrastructure for seniors that led Engskov to found Rippl Care. Rippl is designed to provide seniors as well as their families with behavioral health support, with everyday check-ins, including navigation and therapy. Rippl provides care through "pods," dedicated support teams that consist of a care coordinator, a psychiatric nurse practitioner, and a licensed clinical social worker assigned to each patient. Everyone involved in the patient's care including the patient, family caregivers, the patient's own medical providers, and the pod work together as a team to provide preventative care and intervention when needed. Delivered mostly virtually, Rippl provides 24/7 support to caregivers, whether the patient is living with caregivers in their home or in an assisted living facility. The care focuses on prevention, providing patients and caregivers with the support and guidance they need to avert crises. Engskov and his team called on McLean early in the

company creation stage to see what the hospital might be able to provide in terms of best practice and care protocols for which they are widely known.

“The interventions that Rippl is developing are based on evidence-based practices,” Forester says. “A lot of the work is aimed at teaching the caregivers to care smarter, not harder, and teaching them the basic principles of resiliency. So, when a crisis occurs, they call us instead of going to the emergency room, and we can put them on the phone with a nurse practitioner who can triage and talk the patient and team through the crisis.” With an experienced support team already familiar with the caregivers and the patient, Engskov thinks that most visits to the ER can be avoided, along with the associated trauma and expense.

Rippl is just completing their operations planning and treated their first patient in January near their headquarters in the state of Washington. The company has hired and is training specialists and has signed up a number of care facilities and home health companies, as well as recruited a patient family advisory panel.

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— Kris Engskov

we’re creating one for them. We’re going to develop a platform to let them go out and do the things that they got into medicine to do.”

One of Engskov’s priorities is making Rippl equitable to people in currently underserved areas and to people who can’t afford to pay for care themselves. “We’re not trying to create a concierge company for people with a lot of resources; we’re trying to create a company that can dramatically expand access to these critical, specialty resources to seniors, regardless of their background, their geography, their care environment...”

The company is also advocating for insurance companies to cover the service by sharing risk in value-based arrangements. Currently most behavioral health care is self-paid. Rippl argues that insurance should cover their services because they offer a superior and far cheaper to the existing paradigm of ambulances, emergency room visits, and acute hospitalization.

The average annual per capita Medicare spend is an estimated \$17,000 higher for seniors with Alzheimer’s and other dementias than for those without, mainly driven by the extraordinary cost of emergency treatment. With the Rippl solution, patients and caregivers should experience fewer crises, reducing traumatic experiences for patients and caregivers, and reducing overall spending for families and insurers.

Rippl’s base is in Seattle, but Kris is already planning ahead, with a goal to offer the company’s services nationwide. Rippl intends to build on the paucity of coverage now in place – “right now, the only resource for a lot of families and assisted living facilities is 911.”

Rippl’s biggest challenge is hiring specialists in the midst of a nationwide provider supply shortage. Rippl is addressing this in two ways, first by making the company attractive to potential employees. “We spend a lot of time architecting the platform, place and culture where if you’re drawn to this space and you have the license, you’re not going to want to work anywhere else. The question we ask ourselves is how do we empower the folks who love this population and have the skills to serve them?”

Second, Rippl is developing a training program, in collaboration with Forester and McLean Hospital to find professionals in other disciplines who have the licensure and the passion and train them to work with the target patient population. “There are many people out there who are deeply passionate about working with the elderly, and I don’t think they have a home, so

Funding updates

Mass General Brigham Ventures plays a critical role in founding and funding next-generation technologies. Since inception in 2008, we have invested approximately \$200 million in 55 venture start-ups. The current portfolio includes a number of transformational companies focused on CNS/neurological disorders, immunology, and gene and cell therapy.

Mass General Brigham Ventures has created eight public companies as follows:

IPO Scorecard

MGBV Public Companies	Mkt Cap (\$M)
Akouos, Inc. (AKUS) ¹	\$487
Denali Therapeutics (DNLI)	\$3,687
Editas Medicine (EDIT)	\$623
Keros Therapeutics (KROS)	\$1,466
Magenta Therapeutics (MGTA)	\$49
Spero Therapeutics (SPRO)	\$77
Translate Bio (TBIO) ²	\$3,200
Verve Therapeutics (VERV)	\$1,170
Total Value (2/28/23)	\$10,759

Notes:

1 Acquired by Eli Lilly Dec 2022

2 Acquired by Sanofi Sep 2021



\$450M

Capital Under Management

Key Statistics

- 55 Start-ups since inception
- 16 Exits
- 24 Active companies
- 8 Public companies

M&A activity

Eli Lilly Acquires Akouos in \$487 Million Transaction to accelerate gene therapies

On December 1, 2022, Eli Lilly completed the acquisition of Akouos. The deal included \$487 million in up-front cash and contingent value rights for an aggregate amount of up to \$610 million. Akouos was developing targeted adeno-associated viral (AAV) vector-based gene therapies for sensorineural hearing loss, based in part on work from Luk Vandenberghe at Mass Eye and Ear. The technology has the potential to restore, improve and preserve hearing. Mass General Brigham Ventures joined 5AM Ventures and NEA in seeding the company in 2017 and Akouos went public in June 2020. Akouos had a lead program in the clinic for AK-OTOF, gene therapy for OTOF-mediated hearing loss.



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Recent investments

Amolyt Pharma

On January 6, 2023, Amolyt Pharma closed a €130 million (USD \$138M) Series C equity financing. Amolyt is a clinical stage company poised to deliver life-changing treatments to patients suffering from rare endocrine and metabolic diseases. Amolyt's lead program, a parathyroid hormone analog, originated from Thomas Gardella, John Potts, Michael Mannstadt, and Harald Jüppner in the Department of Endocrinology at Mass General Hospital.

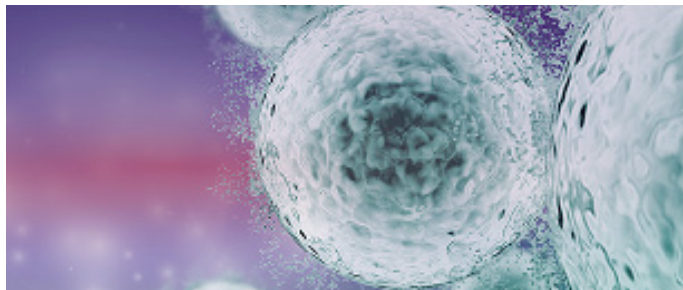
The financing was co-led by Sofinnova Partners and Intermediate Capital Group (ICG) and joined by Novo Ventures, Kurma Partners, EQT Life Sciences, Innobio, Sectoral Asset Management, Pontifax, Orbimed, and Mass General Brigham Ventures.



Amolyt plans to use the proceeds to advance its pipeline of therapeutics for rare endocrine and related disorders, including AZP-3601, now known as eneboparatide, for the treatment of hypoparathyroidism, and AZP-3813 for the treatment of acromegaly. AZP-3601 is currently in Phase III and AZP-3813 is in Phase II(a). In February, Amolyt further expanded its portfolio through a licensing agreement with XOMA to advance pre-clinical development of anti-PTHrP monoclonal antibodies as potential treatments of primary hyperparathyroidism (PHPT) and humoral hypercalcemia of malignancy (HHM).

Garuda Therapeutics

In February, Garuda closed a \$62 million Series B round. Garuda is developing off-the-shelf, self-renewing blood stem cells designed to provide patients with rapid and broad access to consistent, durable, HLA-matched transgene-free blood stem cell therapies. Similar to bone marrow transplants, Garuda's technology has the potential to address, and possibly cure, more than 70 diseases. It also overcomes many limitations of current practices which rely on donor matches which, among other issues, often creates barriers for racial minority and mixed-race patients. The Series B financing was led by Northpond Ventures, OrbiMed, Cormorant, and Aisling, along with



participation from Mass General Brigham Ventures, Sectoral Asset Management, and Alexandria Venture Investments. In conjunction with the closing, Ray Kelleher, M.D., Ph.D., from Cormorant and Mass General Hospital, joined the board.

Garuda was founded by Dhvanit Shah, Ph.D., who previously served as a Principal Investigator at Brigham and Women's Hospital and on the faculty of the Harvard Stem Cell Institute. Other prominent scientific founders include David Scadden, M.D. at Mass General Hospital, Co-Director of the Harvard Stem Cell Institute and Professor of Medicine at Harvard University, as well as Sean Morrison, Ph.D. of Children's Medical Center in Dallas, TX.

The potential of Garuda's breakthrough platform technology is significant, and this funding milestone brings the company one step closer to delivering life changing cellular therapeutics to patients. Garuda's first two programs are slated to hit the clinic in 2024 – these include transfusion-dependent beta-thalassemia (TDBT) and anemias associated with bone marrow failure.

Market Outlook

Public biotech stocks have significantly underperformed the broader market since their peak in Feb 2021, and have been trading sideways over the past six months. The volatility has been driven by macroeconomic factors as inflation, interest rates and banking crises continue to dominate the headlines. On the private side, venture-backed investment activity remained resilient in 2022 but exit activity dropped, with the lowest level of venture backed IPOs since 2012. These challenging conditions have forced companies to optimize resources and prioritize assets to attract more capital. We are hopeful that will see a pickup in M&A activity in 2023, with Big Pharma looking to restock their pipelines. While short term remains fraught, long-term industry fundamentals are solid, with continued innovation driven by small companies and new modalities.