

PAVmed:

A Small Cap Puts Its Streamlined Development Model to the Test

Getting Wall Street to pay attention to micro- and small-cap companies like PAVmed is difficult, particularly in the medtech field. But with the pending IPO of its Lucid subsidiary and formation of a new one focused on digital health, the company, which has a streamlined model for device innovation, has a near-term opportunity to raise its profile.

► WENDY DILLER

At the risk of stating the obvious, most device companies were hurt by the pandemic, largely because of the temporary shutdown of elective procedures and, even after they resumed, it was at a lower rate than normal, a trend that continues. The chief exceptions were areas like diagnostic testing, remote patient monitoring, and other forms of telemedicine. While **Avail Medsystems Inc.** clearly falls into the latter exception,

CEO Daniel Hawkins did not anticipate that COVID-19 would significantly spur Avail's growth. "In the early stages of the pandemic, I told my VP of sales that, if this situation continues, we might get requests from vendors who are locked out of hospitals, but I didn't anticipate the degree to which COVID would cause our business to accelerate," Hawkins recalls. "We ended up with vendors coming to our website in numbers that we never could have imagined."



About seven years ago, the cardiothoracic surgeons and former colleagues Lishan Aklog, MD, and Brian DeGuzman, MD, along with Michael Glennon, an experienced medical device executive, decided to form a company devoted to medical device innovation, building on Pavilion Holdings Group, an earlier successful venture they had started in 2008. They formed **PAVmed Inc.** to develop innovative devices and start-ups based on a fast-to-market, capital efficient business model.

PAVmed aimed to expand upon a model that they had used earlier to sell a company, Vortex Medical, to **Angiodynamics** for \$55 million, plus earn outs of up to \$20 million. Vortex, which sold a device that Aklog invented for clearing large blood clots, *AngioVac*, undertook a single \$3.5 million financing to pay for *AngioVac*'s development from concept to commercialization and generated a minimum 800% return to investors in less than five years, says Aklog.

The rewards from the Vortex sale were substantial but, just as importantly, they provided the founders with credibility. Entrepreneurs and clinician-inventors across the spectrum began seeking out the Pavilion founders for support and advice.

As a result of their Vortex homerun, "there were opportunities to cross-pollinate good ideas from one field to another, so we did not want to pigeonhole ourselves into any one specialty," recalls Aklog, who is

Chairman and CEO of PAVmed. DeGuzman is its Chief Medical Officer and Glennon, who now is CEO and president of another of the earlier venture's portfolio companies, **Saphena Medical**, is Vice-Chair of PAVmed's board of directors.

Initially, access to funding was tough. Medtech continually lags other life sciences subsectors when competing for investor attention. Further, the company did not fit traditional venture capital models, given the structure of its deals and its founders' emphasis on streamlined operations and timetables. At the time, however, a small group of well-connected bankers were advocating for small companies to have better access to public markets, providing PAVmed with a window to go public. The company raised \$5.3 million in an IPO in 2016.

Nevertheless, the founders felt that their top-tier clinical experience and skills learned from the Pavilion venture would serve them well. The surgeons met as residents at Brigham & Women's Hospital in Boston and had deep networks in academic medicine, which gave them early access to innovations and an excellent understanding of clinical needs, plus the ability to attract talent for particular projects, as needed. "We have a concentric ring around us of high-powered folks who come from regulatory, legal and technical backgrounds and understand the value of innovation, and other folks in our networks are no more than one call away from answers on due diligence questions," says Aklog.

The idea was to acquire technologies that address unmet medical needs in potentially large markets. PAVmed is currently pursuing opportunities, ranging from a minimally invasive treatment for carpal tunnel syndrome, *CarpX*, and innovative infusion therapy devices, as well as a next-generation digital oncology monitoring platform company, acquired in June, **Oncodisc** (see Figure 1). The furthest along and biggest project to date is priming its major subsidiary, **Lucid Diagnostics**, for an initial public offering at a date to be determined. Lucid has developed a suite of products for detecting and treating patients with Barrett's Esophagus (BE), a precancerous condition that puts people at high risk of esophageal adenocarcinoma (EAC) cancer.

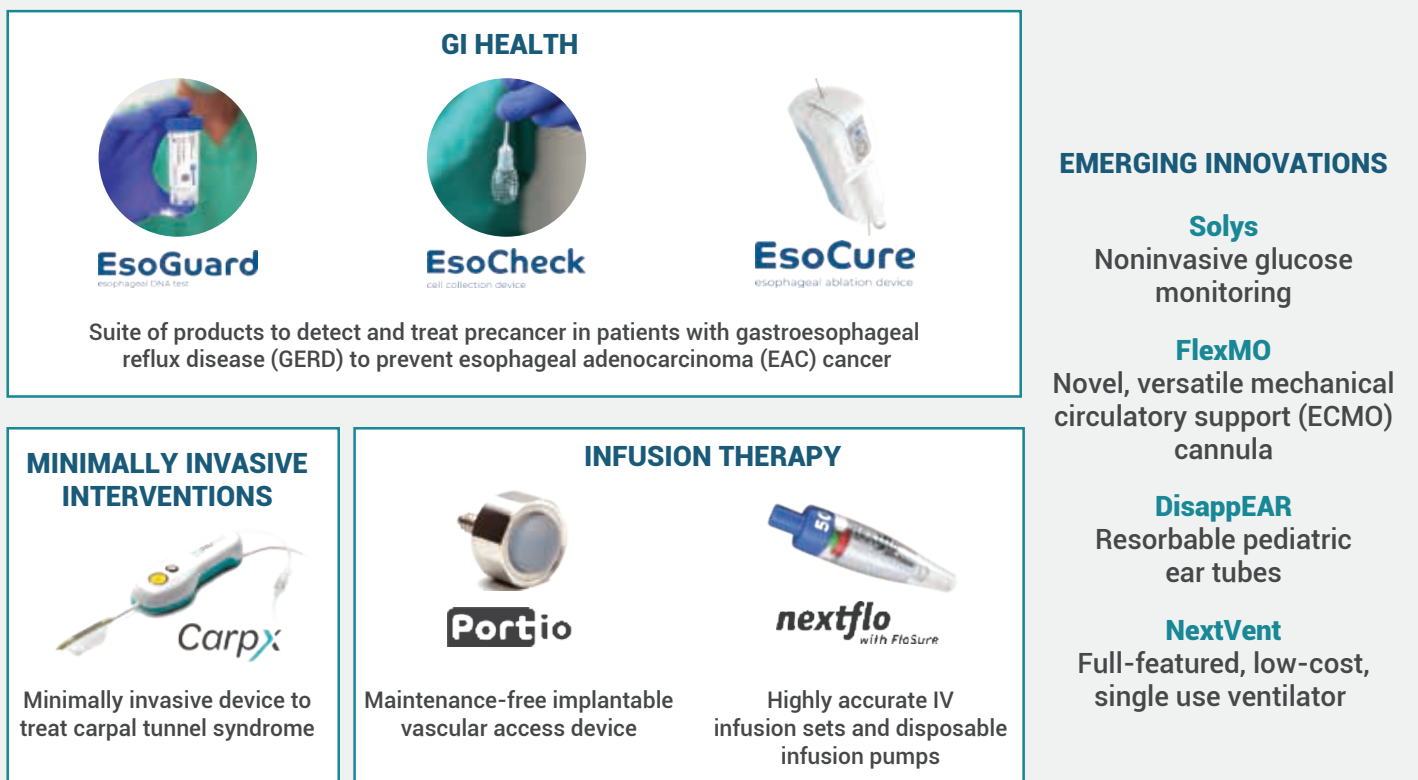
The challenge for PAVmed now is how to obtain broader recognition on Wall Street and, in particular, that of institutional investors, which now comprise only 30% of its investor base. In addition to the usual problems associated with following micro and small-cap companies [at a \$600 million market cap, PAVmed is at the low end of small cap], analysts struggle with placing valuations on small-cap companies with diversified portfolios like PAVmed's. Aklog acknowledges that

achieving a following is "a lot harder than if we were a single-product company, but we have been able to make that case increasingly with institutional investors and consummated the financing deals rapidly."

The diversified, generalist structure of the company is an advantage because PAVmed can "pounce on opportunities," he argues. Lucid, which PAVmed created when its executives had no experience with diagnostics, has been "wildly successful," proving that "refusing to be pigeon-holed into specific sectors" works to PAVmed's advantage. Successfully priming it for an IPO will unlock value for both Lucid and PAVmed, while freeing the latter to raise capital for its other projects, including Oncodisc.

PAVmed's valuation has tripled in the past year, and in the first quarter of 2020, it raised roughly \$75 million through direct registrations and a follow-on offering, bringing its total funding to date to about \$150 million, he points out. While that figure seems small for a public company in the booming life sciences sector, with demonstrated proof of commercial viability of its products, and the pending Lucid IPO, established institutional investors are paying more attention to the intrinsic value of

Figure 1
PAVmed's Product Portfolio



Source: PAVmed

PAVmed's assets, he says. If that translates into access to more capital, the company will have the resources to pursue bigger deals, with longer, more rewarding exit horizons.

PAVmed's Appeal to Case Western

Lucid is an opportunistic play in clinical diagnostics and the farthest in PAVmed's product portfolio from its founders' core expertise. It is also the first real test of the ability of PAVmed's streamlining strategy to create value, and its trajectory shows how the flexible operating processes and top-tier connections can serve to the company's advantage.

In 2018, PAVmed licensed from Case Western Reserve University (CWRU) rights to a pair of non-endoscopic, office-based technologies for detection of BE and EAC. People with chronic heartburn, or GERD, are at risk of developing BE, a premalignant condition in which the cells lining the esophagus are damaged.






While BE is curable, a widely-used screening tool for identifying it does not exist, and incidence of EAC has more than quadrupled in the past 30 years, with a less than 20%

survival rate at five years. The only screening option to detect BE requires performing esophagogastroduodenoscopy (EGD), which is expensive, hard on patients, and impractical. Thus, BE remains undetected prior to about 95% of EAC cases, according to a paper published in 2018 in *Science Translational Medicine* (STM) by authors Sanford Markowitz, MD, PhD, the Ingalls professor of cancer genetics at CWRU's school of medicine and medical oncologist at University Hospitals (UH) Cleveland Medical Center, along with Amitabh Chak, MD, a gastroenterologist affiliated with the University Hospitals Health System in Cleveland, and Joseph Willis, MD, a professor of pathology at CWRU (see Figure 2). All three are co-inventors of the technologies that PAVmed in-licensed.

Despite the urging of a long-time acquaintance, Daniel Simon, MD, the president of UH and a professor at CWRU's medical school, the surgeons initially hesitated. They worried about their lack of diagnostics experience and the absence of published clinical data to support the clinical utility of the devices. Five months later, after publication of the STM paper, and, as interest from corporate competitors surged, Aklog and DeGuzman pursued the deal and won.

Figure 2
EAC Precancer Screening: EsoGuard & EsoCheck

FIRST AND ONLY COMMERCIALY AVAILABLE ALTERNATIVE TO ENDOSCOPY SUITABLE FOR WIDESPREAD EAC PRECANCER SCREENING

	ESOGUARD + ESOCHECK	UPPER GI ENDOSCOPY	CYTOSPONGE + TFF3	TRANSNASAL ENDOSCOPY	CAPSULE ENDOSCOPY
					
Non-invasive	Yes	No	Yes	No	Yes
Venue	Any Office	Endo Center	Any Office	GI Office	GI Office
Capital Equipment	No	Yes	No	Yes	Yes
Total Procedure Time	< 5 min	1-2 hours	10-15 min	15-30 min	Days
Recovery	None	1 day	None	None	None
Highly Accurate	Yes	Yes	No	No	No
Automatable	Yes	No	No	No	No
Commercially Available	Yes	Yes	No	Yes	No
Widespread Screening Tool	✓	✗	✗	✗	✗

Source: PAVmed

Lucid Diagnostics' planned IPO would be the first real test of the ability of PAVmed's streamlining strategy to create value, and its trajectory shows how the flexible operating processes and top-tier connections can serve to the company's advantage.

"Case Western has a successful track record in out-licensing technologies, and the head of the technology transfer office took a bet on us," recalls Aklog. Still, the founders' pedigree, focus and emphasis on operating efficiency, appealed to CWRU and the inventors involved, who were eager to achieve clinical as well as commercial success. PAVmed also offered a differentiated deal structure, which including forming a separate subsidiary to develop the technologies. The terms enabled both the university and the faculty inventors to obtain royalty streams, as well as a combined meaningful equity stake in the subsidiary that would not be subject to dilution until an IPO. And, unlike VC investors, which walk their portfolio companies through multiple rounds of financings and uncertain future dilution, the PAVmed terms required CWRU to take its entire dilution upfront, with a higher than traditional floor. In addition, the deal eliminated the standard termination clause that can be exercised by a university when a licensee fails to meet milestones, and is replaced with a call option.

"PAVmed offered a unique combination of entrepreneurship and financing stability," says Stephanie Weidenbecher, a senior

licensing officer at CWRU's tech transfer office, and director of its Validation and Start-Up Fund, who has played a key role in facilitating the deal. Start-ups generally take a few years to raise funding before they have resources to support product development through commercialization, but PAVmed agreed to commit the funding and management expertise upfront that enabled Lucid to hit the ground running, she notes. "We wanted a start-up mentality with financial backing, and the ability to start work immediately, all of which they offered."

While Aklog and DeGuzman lacked diagnostics expertise, they assembled a group of strategic advisors which include some of the industry's most successful leaders. These include Stanley Lapidus, the founder and former president of Cytyc, which revolutionized cervical cancer detection and screening, and the founder and former Chair and CEO of Exact Sciences, which has had a similar impact on screening for colorectal cancers. In addition, Alberto Gutierrez, PhD, a well-known former head of the FDA Office of In Vitro Diagnostics & Radiological Health, who is now an expert advisory at NDA Partners, a consulting firm, and Nicholas Shaheen, MD, a professor of medicine at the University of North Carolina School of Medicine and Chief of GI and Hepatology at UNC Healthcare, are advisors. Shaheen, who is also a co-author of the current guidelines endorsed by GI professional societies for management of BE, is Chair of Lucid's medical advisory board and the principal investigator for its pivotal study of Lucid's *EsoGuard* molecular test. Markowitz, Chak, and Willis are co-founders and Chak and Markowitz remain as advisors to Lucid.

Beating Back Esophageal Cancer

Lucid's ultimate goal is to provide an integrated suite of technologies to address all aspects of BE and EAC less invasively and more accurately, eliminating or reducing the need for repeated endoscopies, says Aklog. The technologies it licensed from Case Western are designed to replace endoscopy as a screening tool.

The *EsoCheck Cell Collection Device* is a miniaturized balloon catheter designed to collect cells from a targeted region of the esophagus in a five-minute non-invasive office-based procedure, which can be conducted by a trained technician, including auxiliary healthcare providers. *EsoGuard* is a molecular test targeting the VIM DNA and CCNA1 methylation biomarkers, which the 2018 STM validation study determined has greater than 90% sensitivity and specificity for discriminating BE from normal tissue when combined with *EsoCheck*. *EsoCheck* has been FDA cleared via the 510(k) process, while *EsoGuard* has been given breakthrough designation by the FDA and is available through the company's CLIA-certified laboratory. A pivotal trial that the

company has designed to be the basis of a submission to FDA for PMA approval is now underway (see Figure 3).

Separate from the CWRU technologies, the company also is developing an ablation therapy for curing BE, which it calls *EsoCure*, which is synergistic with *EsoCheck* and *EsoGuard*. This single-use disposable hot-water based technology produces direct thermal injury as a less expensive and effective alternative to currently available ablation devices sold by **Medtronic plc** and others, which require the use of expensive consoles, says Aklog. The technology is based on intellectual property that PAVmed acquired several years ago for other purposes, but the company has now prioritized it for BE based on its potential to cure that condition. It has been successfully tested in animal models, and the plan is to submit it for FDA regulatory approval next year.

An Exact Sciences Parallel?

Lucid's trajectory could be similar to Exact Sciences, the groundbreaking company that developed an at-home molecular DNA screening test for colorectal cancer, founded by Lapidus. "People are starting to understand the opportunity is massive," says Aklog. That said, Exact Sciences was not an overnight success, and has been built up over decades and is based on an investment of tens if not hundreds of millions of dollars in clinical

trials and product development. (See sidebar, "Stan Lapidus on Diagnostics for Early Cancer Detection.")

Lucid believes early BE detection enabled by these technologies addresses a \$25 billion market. To capture this opportunity, it has hired a sales team to grow its commercial reach to GI specialists. In addition, the company is testing the ability of running its own test centers to super-charge adoption outside of the GI specialist channels. These centers—there is a pilot center now operating in Phoenix, AZ—will be staffed by nurse practitioners, who can readily be trained to administer the *EsoCheck* sample collection procedure. Individuals with heartburn can go to these centers to get samples collected, then wait for results as the samples get sent to Lucid's laboratory for analysis. Eventually, the company has plans for direct-to-consumer (DTC) marketing to patients. Although PAVmed operates on a lean budget, the economics fall within its models as medical office space is inexpensive, Aklog says. Nurse practitioners can do up to roughly 20 tests per day, but the break-even point for the centers is much lower, he adds.

To support these programs, this July Lucid entered into a strategic alliance with **UpScriptHealth**, a direct-to-consumer telemedicine company that offers a branded web-based telemedicine platform. The Lucid initiative will be directed at

Figure 3
EsoCheck Esophageal Cell Sampling Procedure

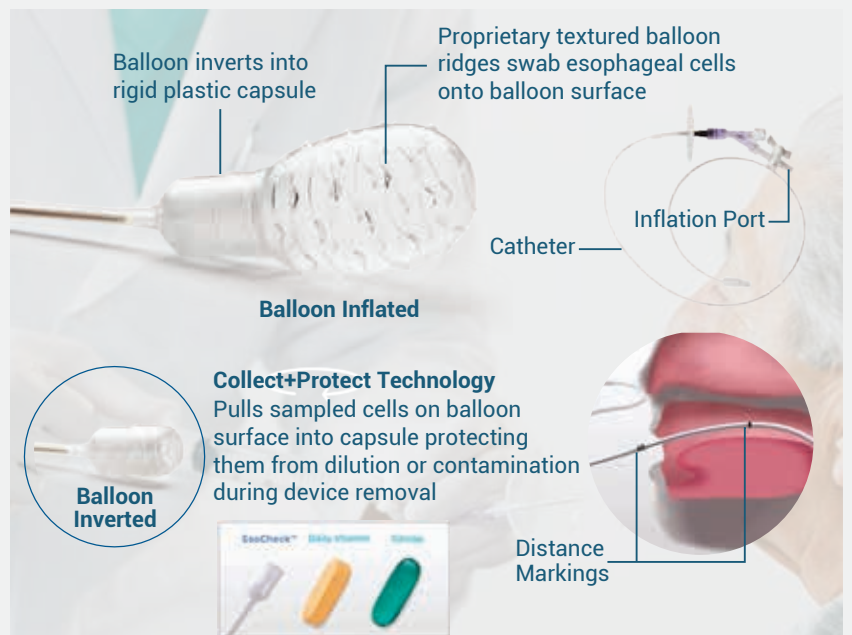
FIRST AND ONLY COMMERCIAL TARGETED & PROTECTED ESOPHAGEAL CELL COLLECTION DEVICE



Simple, <5-minute non-invasive office-based procedure

Targeted sampling of lower esophageal cells

Protection of sampled cells from dilution and contamination during device removal



Source: PAVmed

patients with chronic heartburn symptoms, who can request a video evaluation by a physician and, if indicated, referral to the *EsoGuard* test. The company is also embarking on an initiative to educate consumers on the correlation between chronic heartburn and esophageal cancer and the importance of detecting precancerous lesions that can prevent progression.

Moving Into Digital Health With Oncodisc

While Lucid is PAVMed's nearest term opportunity, and a big factor in its drive for credibility and additional capital, the company's latest acquisition, Oncodisc, has potential to be a just as much of a game-changer. The deal, completed in June, led to the launch of a new PAVmed subsidiary, **Veris Health**, that brings PAVmed directly into the digital healthcare world.

Oncodisc was founded in 2018 by physician entrepreneurs James Mitchell, MD, a radiation oncologist, and Andrew Thoreson, MD, an interventional radiologist, with the goal of designing digital tools for optimizing the delivery of oncology care. The core technology is an implantable vascular access port with built in biosensors and wireless communication for remote monitoring of patients undergoing outpatient chemotherapy to track early warning signs of complications and compliance, says Mitchell, who is now Veris' Chief Medical Officer; Thoreson is an advisor who remains involved in product development. These warning signs include well-established failure-to-thrive parameters, including activity levels, temperature, heart rate, and other metrics.

The product is in development with the goal of offering an easy-to-understand user interface summarizing the patient's condition within a longitudinal trending context. Machine learning and artificial intelligence will be used to automate interpretation of the data to enable the oncologist to provide more accurate, actionable insights, Mitchell adds. The initial product has undergone successful proof-of-concept testing in animals, and the PAVmed deal will accelerate the ability to finalize the design for human clinical trials. Veris expects to file for FDA 510(k) submission in second half of 2022.

Oncodisc is differentiated from many digital health offerings because of its focus on the physician-patient relationship in a well-defined context, says Aklog. By applying digital tools to monitoring the effects of carefully structured chemotherapy regimens, the PAVmed team believes Oncodisc—now Veris—can improve care by decreasing complications, reducing hospital readmission rates, and other metrics which are concrete and easy to measure.


The deal's appeal and its structure were inspired by Lucid, participants say. Oncodisc's founders considered alternatives, meeting with healthcare systems, pharma companies, and

venture capitalists that invest in medtech, but PAVmed's leaders had a common interest in speed and efficiency of development of new devices and a track record of successful exits. Lucid's inventors also were enthusiastic about working with PAVmed's clinically oriented founders, says Mitchell.

They rejected working with big companies that might shelve development of their products, with changes in management and priorities. Besides, the founders' aim was not to duplicate the current price-driven business model for vascular ports, but to package the device and digital platform together, offering them as a subscription-based remote monitoring platform. This can be reimbursed according to existing codes for implantation procedure, plus monthly monitoring fees. There are also opportunities for oncologists to improve their reimbursement through special goal-driven programs that CMS has arranged.

To complete the deal, Veris acquired Oncodisc, giving PAVmed an 80.5% stake in the subsidiary and Oncodisc founders a 19.5% equity position. The deal calls for PAVmed/Veris to assume all development and financing risk, while remaining non-dilutive for PAVmed stakeholders until the IPO or other exit. The preliminary plan is for PAVmed to eventually take Veris public, just as it is doing in the near-term for Lucid.

While a date for the Lucid IPO has yet to be determined, it is expected to be a near-term event and a potential catalyst for creating value for PAVmed. Data on *EsoGuard* is still incomplete, as clinical utility studies have yet to be done, which could affect valuation. And, as the commercial activities roll out, the company believes it will face an easier road than Exact Sciences did with *Cologuard*. First, *Cologuard* competes against well-established procedures as a screening tool, since 60%-70% of people recommended for colonoscopies get them. Therefore, *Cologuard* was seen by some as an end run around GI specialists since it eliminates the need for endoscopy. With Lucid, that is not the case because only 5-10% of eligible people get upper endoscopies for BE screening. In fact, gastroenterologists "embrace *EsoGuard* because our results can direct patients who currently are not screened at all to them for follow up endoscopies," Aklog explains.

The Veris/Oncodisc technology is at an even earlier stage, and still in development, with much of the work focusing on simplifying the user interface. It faces challenges of a different kind, including the novelty of a subscription-based program for oncologists and whether they will find the data derived from the implantable devices overwhelming. But if it works out, PAVmed will be in a different place a year from now. 

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