Evaluate Vantage

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Eclipse plunges Guardant into darkness

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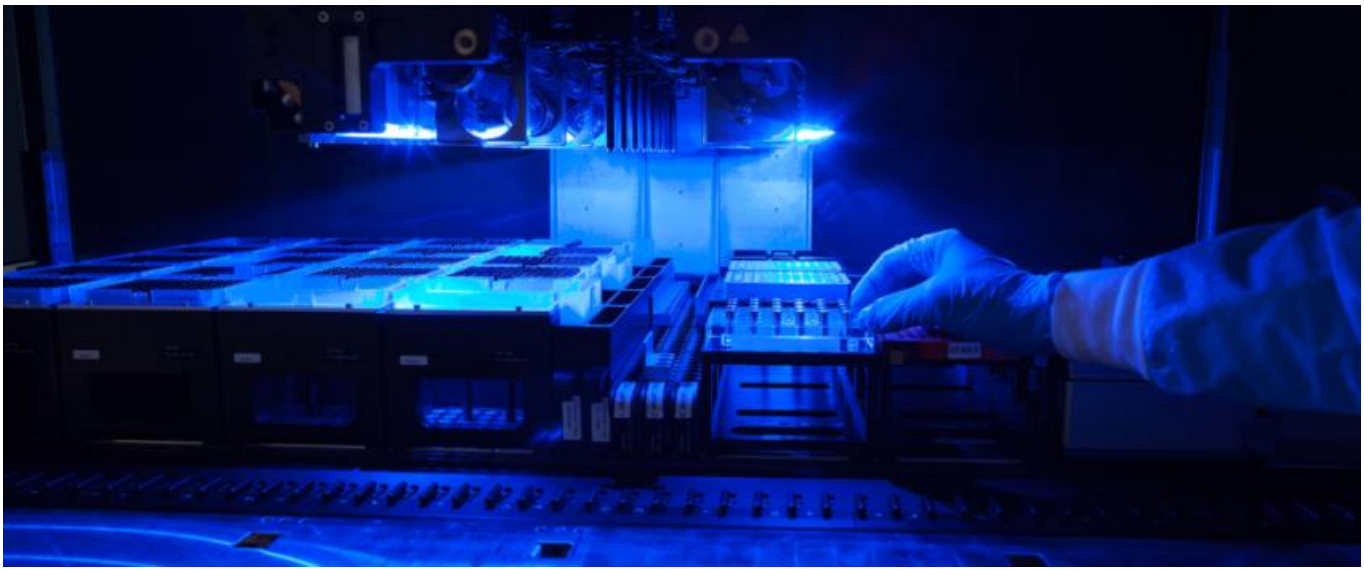

Investors punish the liquid biopsy maker for lacklustre data on its colorectal cancer screen.

Three years, 20,000 participants and untold millions of dollars, and the pivotal trial of Guardant's Shield colorectal cancer screen has turned out a disappointment. Approval is still probable, and even widespread reimbursement for the blood test is on the cards, but the label is likely to be narrower than hoped for.

Guardant's shares were down 31% in early trade today, slicing $1.3bn off its market cap. The misfire means Exact Sciences will remain the leading colorectal cancer screening company, thanks to its faecal test Cologuard. Relieved shareholders sent Exact's stock up 26%, adding nearly $2bn to its market value.

The Shield assay is already sold in the US as a lab-developed test, without FDA oversight. The Eclipse study was intended to secure approval and thus reimbursement of the test, thereby expanding its sales.

Eclipse recruited a vast number of people with no colorectal cancer diagnosis and an average risk of developing the disease. It tested two versions of Guardant's liquid biopsy – a cell-free DNA (cfDNA)-only test and an assay using both cfDNA and protein biomarkers. The cfDNA-only test outperformed the version with protein biomarkers, and the company only revealed data on the better version.

Compared with the gold standard diagnostic method, colonoscopy, Shield, previously known as Lunar-2, detected colorectal cancer with 83% sensitivity. Specificity was 90% in people without advanced neoplasia and in those a who had a negative colonoscopy result. This is a decrease from previous trial results; in data presented at at last year's Asco the assay yielded sensitivity and specificity of 91% and 94%, respectively.

The data cited on Cologuard's label puts Exact's test's sensitivity and specificity at 92% and 87%, respectively.

Second fiddle

It gets worse for Guardant. The test only demonstrated 13% sensitivity in detecting advanced adenomas – benign tumours that can go on to become cancerous. Cologuard's sensitivity here was 42%.

This is the real disappointment, as it might prompt the FDA to omit a claim for advanced adenomas in any label it grants Shield. Alternatively, the agency could mandate that the test only be used once other colorectal cancer screening methods have been refused.

Approval in at least some part of the screening population is fairly likely. If it does come Medicare

reimbursement is all but assured, since the trial results exceed the performance criteria set forth by the Centers for Medicare & Medicaid Services. These call for at least 74% sensitivity and 90% specificity.

Guardant will complete its premarket approval submission to the FDA in the first quarter of 2023, and is targeting approval around a year later, according to SVB analysts. It hopes to be able to price the test at $895.

Guardant reckons the CRC screening market to be worth $20bn, and SVB analysts see liquid biopsies reaching a market share of around 10% of that. Following yesterday's data, they believe Shield could obtain 40% within that, meaning it could eventually see annual sales of around $800m.

By contrast, the sellside forecasts sales of $1.3bn for Cologuard this year, rising to $3.2bn in 2028, consensus data from *Evaluate Medtech* shows. The Eclipse readout might yet prompt analysts to raise this figure. No wonder Exact is riding high.