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August/September 2021 Report

ERASCA

- Erasca Inc. is a clinical-stage precision oncology company that focuses on discovering, developing, and commercializing therapies for patients with RAS/MAPK pathway-driven cancers
- They have now been named one of the industry's most promising biotechnology companies
- In September, Erasca announced a clinical trial collaboration and supply agreement with Pfizer Inc. for the BRAF inhibitor encorafenib (BRAFTOVI®)
    - This agreement will support a clinical proof-of-concept study evaluating ERAS-007, and oral ERK1/2 inhibitor, in combination with encorafenib and the EGFR inhibitor cetuximab for the treatment of patients with BRAF V600E-mutant mCRC
        - This combination of encorafenib and cetuximab was approved in April 2020 for previously treated patients with BRAF V600E-mutant mCRC
        - The combination demonstrated improved overall survival compared to the chemotherapy control arm
    - This combination will be investigated as part of the Phase 1b/2 HERKULES-3 trial expected to initiate in the second half of 2021
    - Erasca will sponsor the study and Pfizer will supply encorafenib
    - The two companies will then form a Joint Development Committee to review the clinical trial results
- Later in the month, the company announced dosing of the first patient in the HERKULES-2 Phase 1b/2 trial evaluating ERAS-007 in combination with various agents in patients with advanced non-small cell lung cancer
    - HERKULES-2 is a master protocol designed to inhibit multiple oncogenic drivers of the RAS/MAPK pathway to address high unmet needs in lung cancer
    - The focus will first be on patients with mutant EGFR or KRAS NSCLC
    - HERKULES-2 will initially examine the safety, tolerability, and preliminary efficacy of ERAS-007 in combination with osimertinib (TAGRISSO®) in patients with advanced NSCLC harboring an epidermal growth factor receptor mutation (EGFRm)
- At the end of the month they announced dosing of the first patient in HERKULES-3, a Phase 1b/2 master protocol clinical trial evaluating ERAS-007 in combination with various agents in patients with gastrointestinal cancer, with initial focus on patients with advanced colorectal cancer
    - The initial focus is on CRC subtypes with BRAF V600E, KRAS, or NRAS mutations
    - HERKULES-3 will examine the safety, tolerability, and preliminary efficacy of ERAS-007 in combination with other cancer therapies in study participants with GI malignancies

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- The dose escalation portions of the first two sub-studies will assess ERAS-007 in combination with the current standard of care, encorafenib (Braftovi®) and cetuximab (Erbitux®), in patients with BRAF V600E-mutant mCRC, and ERAS-007 in combination with the CDK4/6 inhibitor palbociclib (Ibrance®) in patients with KRAS- or NRAS-mutant mCRC
- The Phase 2 dose expansion portion will further evaluate the safety and efficacy of each combination at the recommended dose identified in patients with previously treated mCRC
- Future sub-studies of HERKULES-3 will explore ERAS-007 in combination with other agents in patients with different mutational subtypes of GI cancers.

Amazon and Healthcare

- In July 2021, Amazon launched Dx, a service that offers at-home testing for COVID-19
    - Consumers order a kit off **amazon.com** and send it back for testing and results within 24 hours
- Amazon is looking to expand its medical diagnostics operations on a global scale
    - The company's aspirations are evident in their recent job postings - ex. A position for a medical regulatory officer to be based in Seattle where the headquarters are based
        - The medical regulatory officer would work with developers of new diagnostic tests or processes and serve as the sole contact with key regulators, building relationships with agencies
        - They would also build a team to monitor changes in local, state, and federal/ national regulations, and manage the team to drive revised or new process changes to maintain regulatory compliance

Amazon Care

https://amazon.care

- Amazon stated that they have attracted multiple companies that are interested in using its telehealth service, Amazon Care
    - One of which is Precor - a Washington-based fitness equipment company that was acquired by Peloton
- The service started as a pilot program for employees in and around the Seattle area and provides virtual urgent care list and free telehealth consults and in-home visits from medical professionals
- Other services Amazon Care offers:
    - In-app text chat with clinicians
    - Prescription delivery from a care courier
- In March, the company announced that it would expand the virtual care part of the program nationally for its employees and other companies starting this summer
    - Their plan is to expand its services to more than 20 major U.S. cities this year and in 2022

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- To start, the added in-person services will only be offered in Washington state and metro areas including Baltimore and Washington, D.C.
- The company's vision is to make the full Amazon Care service abatable to other parts of the country, including rural areas
    - Thousands of employees will need to be hired to reach this scale

Amazon invests millions in a pre-revenue company with a system for measuring human proteins - Aug. 5, 2021
https://www.cnbc.com/2021/08/05/amazon-invested-millions-in-nautilus-biotechnology.html
- Amazon has invested millions in a pre-revenue biotechnology company, **Nautilus** Biotechnology, that went public after merging wit ha special-purpose acquisition company in early June
- This move fits Amazon's efforts to build a presence in health care:
    - They now operate an online pharmacy called Amazon Pharmacy, following the $753 million acquisition of start-up PillPack in 2018
    - Last year, they partnered with employee health provider Crossover Health to launch neighbourhood health clinics for warehouse workers and their families in a handful of cities a
    - They have a telehealth service called Amazon Care which was launched in 2019 as a pilot program for employees
- Nautilus has built a prototype for a device that can measure the human proteome, which is constantly changing based on food consumption and other factors
- Organizations could use Nautilus' system for drug discovery, as well as clinical diagnostics and precision medicine
    - Studying the proteome could also help researchers find treatments for people who end up with severe lung damage after contracting COVID-19
- In 2020, Genetech agreed to use Nautilus' system
- Jeff Bezos' venture-capital firm, Bezos Expeditions, also invested in Nautilus as well

Nautilus
https://www.nautilus.bio
- Nautilus' vision is to bring to market a complete, end-to-end, massive-scale protein analysis platform
    - Their hope is that in the same way that democratizing access to the genome was a catalyst for the development of a broad and vibrant genomes ecosystem, the Nautilus' proteomics innovation will unlock high-value applications in precision and personalized medicine, drug discovery, and diagnostics
- The Nautilus Proteomic Analysis Platform leverages a nano fabricated, large-scale, single-molecule protein array, multi-cycle imaging, and machine learning analysis to potentially identify and quantity the proteome with extreme sensitivity and scale

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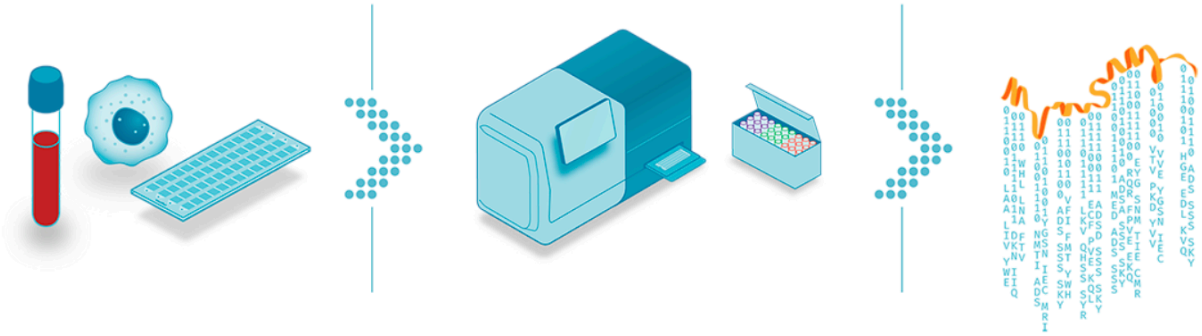
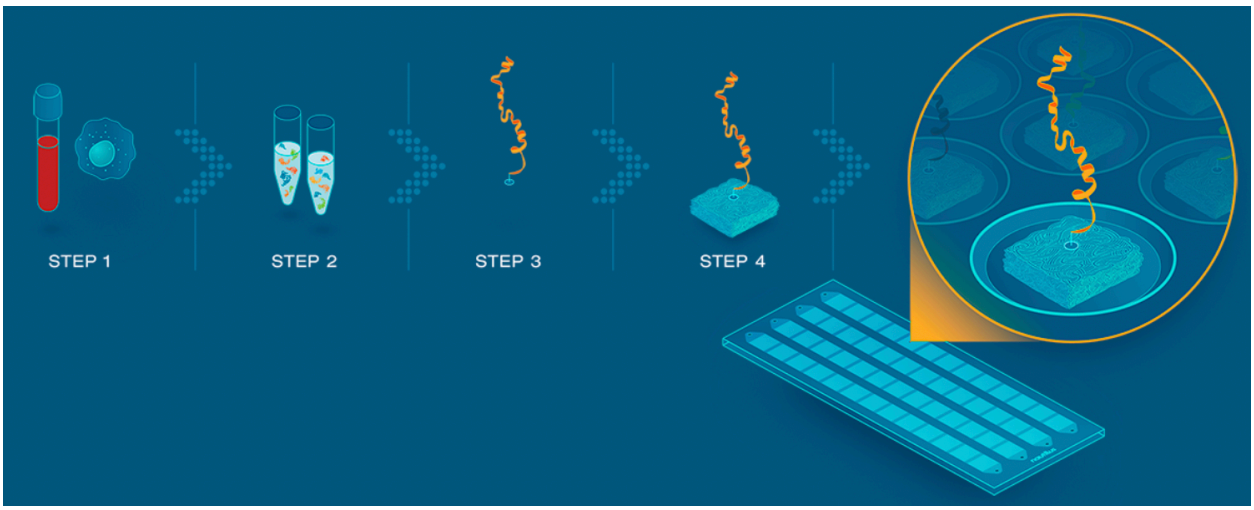
- First, individual, intact protein molecules are immobilized via conjugation to proprietary scaffolds for deposition onto an array with billions of landing pads
- Next, multi-cycle imaging allows repetitive, non-destructive probing of individual proteins with unique binding reagents
- The results are digitized and analyzed to decode the proteome, potentially enabling quantitative analysis at unprecedented scale over an exceptionally large dynamic range



- Isolated protein from blood, tissue, or cells is bound to a proprietary scaffold for single-molecule, single-protein deposition onto one of the 10 billion landing pads found on the Nautilus array
    - The array's hyper-dense surface is designed with the goal of allowing identification and quantification of millions of individual protein molecules simultaneously



- The protein array is loaded onto the platform where fluorescent affinity-probes flow over the array to bind short, defined protein motifs and binding events are measured

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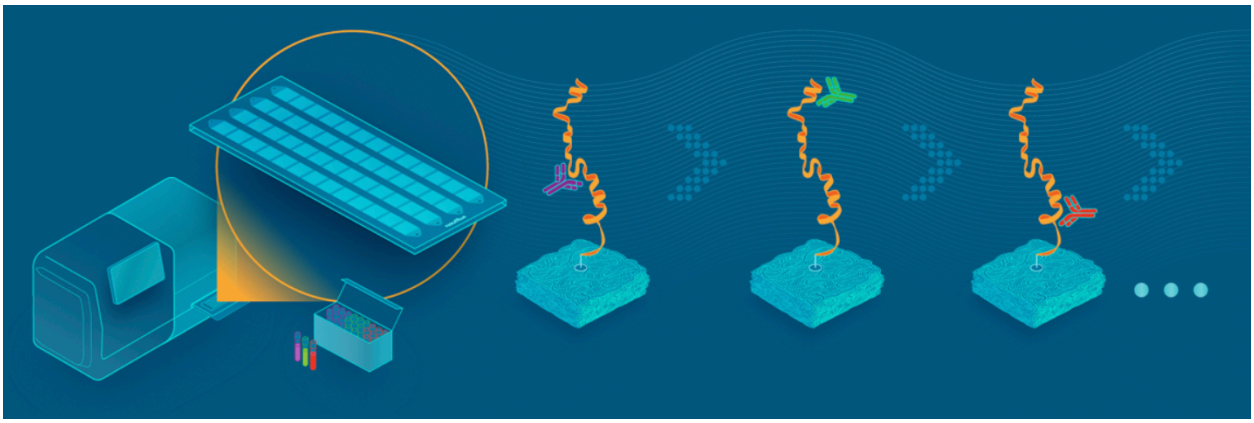
- Since samples are not degraded, they can be washed and probed repeatedly with a variety of unique affinity-probes, each designed to target specific motifs on multiple proteins
- Every new cycle provides unique information and increases the resolution of individual protein identity
- Using this approach, the platform aims to sensitively measure tens of billions of molecules across hundreds of cycles in a day



- Their machine-learning analysis software is designed with the goal of converting binding information to protein identifies and quantities
- The binding results from each cycle are digitized and the Nautilus software is used to decode the binding sequence into broad-scale proteomics information
- As the database grows, the systems' ability to decode the proteome will continually improve

- Second Quarter 2021 Financial Results
    - Operating expenses were $10.7 million
        - 215% increased from $3.4 million in June 2020 - increase in operating expenses mainly due to increase in headcount to support ongoing development of products and for costs associated with being a public company
    - Net loss was %10.7 million
        - Compared to a net loss of $3.4 million for the corresponding prior year period
    - Cash, cash equivalents and investments: $338.4 million as of June 30, 2021
- In June, Nautilus completed a business combination transaction with ARYA Sciences Acquisition Corp III and became a publicly traded company
    - Gross proceeds from this transaction totalled approximately $345.5 million

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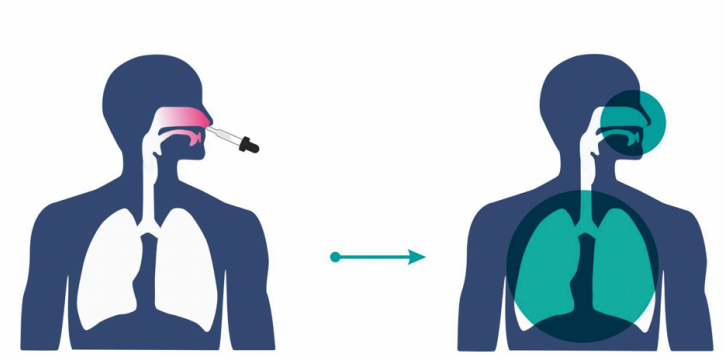
Pandemic driving capital into the biotechnology sector

- Increased interest in the novel technology during the pandemic has driven a lot of capital into the biotechnology sector
    - This has fuelled record financings and IPOs
    - The iShares Biotechnology ETF, which tracks the biotech industry's biggest players has surged roughly 62% over the last 2 years
    - This beat the performance of the S&P 500, which has jumped by about 47% over the same time period

BBV154 by Bharat Biotech

https://www.bharatbiotech.com/intranasal-vaccine.html

- Indian vaccine maker Bharat Biotech's nasal COVID-10 vaccine candidate, BBV154, has received regulatory approval to conduct a Phase II clinical trial
- BBV154 is a novel adenovirus vectored, intranasal vaccine for COVID-19



    - The intranasal vaccine stimulates a broad immune response - neutralizing IgG, mucosal IgA, and T cell responses
    - The idea is that the nasal route has excellent potential for vaccination due to the organized immune systems of the nasal mucosa and immune responses in the nasal mucosa is essential for blocking both infection and transmission of COVID-19
    - The vaccine increases the ease of administration as it does not require trained health care workers
    - They also believe they are able to meet global demands with scalable manufacturing

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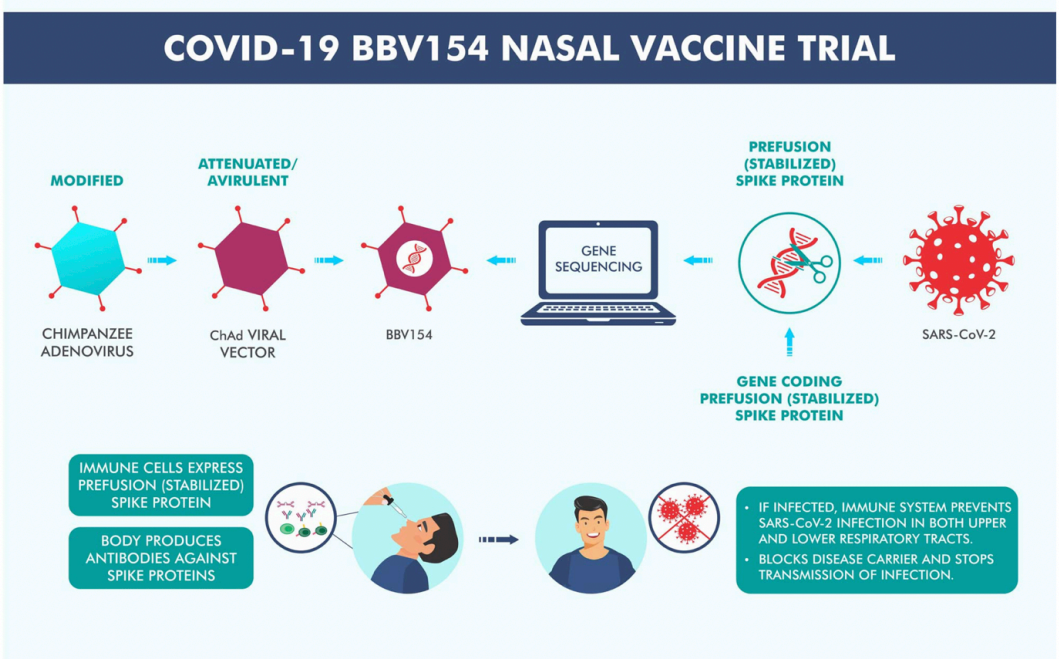

-The vaccine candidate has been completed in subjects aged 18 to 60 years and the doses were found to be well tolerated
    - Mice, hamsters, and macaques that were immunized with a single dose of the vaccine candidate demonstrated superior protection against SARS-CoV-2 challenge and post challenge, viral clearance was observed in both lower and upper airways in all animal models
- The company also has COVAXIN, an injectable COVID-19 vaccine that has already been approved for emergency use approval in India
    - The vaccine was developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV)
    - The vaccine is developed using Whole-Vision Inactivated Vero Cell derived platform technology
        - Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects
        - They contain dead virus, incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection
        - Conventionally, inactivated vaccines have been around for decades and numerous vaccines for diseases such as Seasonal Influenza
    - COVAXIN® is included along with immune-potentiators, also knows as vaccine adjuvants, which are added to the vaccine to increase and boost its immunogenicity
    - It is a 2-dose vaccination regime given 28 days apart
    - No sub-zero storage is required - it is stable at 2-8°C

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- Pre-clinical studies demonstrated strong immunogenicity and protective efficacy in animal challenge studies conducted in hamsters and non-human primates
- The vaccine received DCGI approval for Phase I and II Human Clinical Trials in July 2020
- COVAXIN® demonstrated 77.8% vaccine efficacy against symptomatic COVID-19 disease, through evaluation of 130 confirmed cases, with 24 observed in the vaccine group vs. 106 in the placebo group
- The efficacy against severe symptomatic COVID-19 disease is shown to be 93.4%
- The efficacy data demonstrates 63.6% protection against asymptomatic COVID-19
- Safety analysis demonstrates adverse events reported were similar to placebo, with 12% of subjects experiencing commonly known side effects and less than 0.5% of subjects feeling serious adverse events.