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# December/January 2023 Report

**BioNTech lines up 5 infectious disease vaccine trials for 2023 -** November 7, 2022
https://www.fiercebiotech.com/biotech/life-beyond-covid-biontech-lines-5-infectious-disease-trials-2023

- BioNtech has a list of first-in-human trials for mRNA vaccines ready to go in the coming months, including BNT163 for herpes simplex virus type 2 (HSV-2), a vaccine for shingles in collaboration with long-term partner Pfizer, and a malaria vaccine (BNT165)
- In it's third-quarter earnings results, the company also announced that the first patient should receive the BNT164 vaccine for tuberculosis early 2023
- BioNTech's oncology pipeline is also well underway
    - The company has 19 candidates across a total of 24 clinical trials, including CAR-T cell therapy candidate BNT211.
    - The furthest developed are phase 2 trials of melanoma vaccine BNT111 and BNT113 for HPV16-positive cancers—which both use the biotech's FixVac platform—plus a pancreatic cancer hopeful called autogene cevumeran and the bispecific antibody immune checkpoint modulator BNT311.
    - There is one final cancer readout to come this year in the form of the BNT312 combination therapy in patients with advanced solid tumors, which will be presented at the ESMO immuno-oncology annual congress in December

**NeoGenomics Growing Evidence Base for Residual Disease Assay in Breast Cancer** - December 12, 2022
https://www.precisiononcologynews.com/cancer/neogenomics-growing-evidence-base-residual-disease-assay-breast-cancer#.Y7iNby_71pQ

- NeoGenomics has taken new steps in building evidence to establish its blood-based cancer detection assay in the early-stage breast cancer space
- Their platform, called Radar, falls under the umbrella of minimal residual disease or molecular residual disease (MRD) testing
- This tumor tissue-informed, patient-specific sequencing method was developed by Inivata, which NeoGenomics acquired in 2021
    - Each Radar assay is a personalized panel of up to 48 variants that are selected for each patient based on upfront tumor sequencing data
    - The 48 variants are then gauged via sequencing in cell-free DNA extracted from the patient's blood sample
    - Radar is akin to Natera's Signatera, which has been adopted in the setting of colorectal cancer
- NeoGenomics plans to advance Radar across multiple tumor types - they are conducting research in head and neck as well as lung cancers, and breast cancer, which is where the company believes Radar has the potential to shine
- In the breast cancer space, where MRD assays need to be sensitive enough to pick up the presence of mutant alleles at low levels

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- NeoGenomics shared at the San Antonio Breast Cancer Symposium that Radar can detect either residual cancer signal or cancer reemergence across the neoadjuvant, adjuvant, and surveillance settings
- In the c-TRAK TN trial, researchers compared the company's Radar results to a digital PCR approach
    - Patient data in the surveillance setting over a median follow-up of about 22 months were analyzed
    - Investigators reported that Radar detected ctDNA in nearly 40 percent of the 141-patient cohort, compared to about 36 percent for dPCR
    - Eight patients were deemed positive for a cancer signal by Radar but not by dPCR, and two by dPCR but not Radar
    - Five of the eight dPCR negatives went on to relapse, as did one of the Radar negatives
    - The researchers wrote that Radar offered the first hint of recurrence for nearly half of the patients who showed a molecular recurrence in the form of emerging circulating tumor DNA
    - Radar also boasted a longer time between ctDNA detection and relapse than dPCR — a median of 6.1 months versus 3.3 months, respectively
- Investigators also reported preliminary data from a long-term prospective cohort study called TRACER, which is investigating the use of Radar in patients with early breast cancer across multiple subtypes
    - Samples were measured at baseline, during neoadjuvant chemotherapy, surgery, and at post-surgical follow-up
    - Among 98 of the first subjects enrolled, Radar was able to detect circulating tumor DNA in 80 percent at baseline — prior to neoadjuvant chemotherapy — allowing for further monitoring of ctDNA dynamics during treatment and post-surgery

**Medtronic announces first patient enrolled in U.S. clinical trial for Hugo™ robotic-assisted surgery system** - December 15, 2022
https://news.medtronic.com/2022-12-15-Medtronic-announces-first-patient-enrolled-in-U-S-clinical-trial-for-Hugo-TM-robotic-assisted-surgery-system

- Medtronic plc, a global healthcare technology leader, today announced the first patient enrolled in the Expand URO U.S. clinical trial for the Hugo™ robotic-assisted surgery (RAS) system
- The robotic-assisted prostatectomy procedure was performed by Dr. Michael R. Abern at Duke University Hospital in Durham, N.C
- Minimally invasive surgery, including robotic-assisted surgery, offers fewer complications, shorter hospital stays, faster return to normal activities, and smaller scars
- Urologic procedures are one of the most commonly performed with the assistance of a surgical robot

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- The Hugo™ RAS system is intended to be used in this study for urologic surgical procedures including radical prostatectomy, radical cystectomy, and nephrectomy (partial or radical) procedures at sites in the U.S
- The Expand URO clinical trial is being conducted pursuant to an Investigational Device Exemption from the U.S. Food and Drug Administration
    - Up to 122 patients will be enrolled in the study at six sites in the U.S.
    - Dr. James Porter, a urologic surgeon at Swedish Medical Center in Seattle, WA, is the principal investigator of the U.S. Expand URO study
- https://www.medtronic.com/covidien/en-ca/robotic-assisted-surgery/hugo-ras-system/products-and-system.html
- The Hugo™ RAS system is commercially available in certain geographies
    - In Canada, the Hugo™ RAS system has a Health Canada licence
    - In the EU, the Hugo™ RAS system is CE marked
    - In the U.S., the Hugo™ RAS system is an investigational device not for sale

**Development in the Surgical Robotics space in 2022**

https://www.mddionline.com/robotics/surgical-robotics-continue-rapid-expansion-2022

- February: Medtronic announced that a Belgium surgeon had performed the first clinical procedure in Europe using the company's Hugo robotic-assisted surgery (RAS) system
- May: Ethicon, a Johnson & Johnson MedTech company, announced that its Auris Health subsidiary won FDA clearance for its robotic-assisted Monarch platform for endourological procedures
    - The clearance makes Monarch the first and only multispecialty, flexible robotic solution for use in both bronchoscopy and urology
- May: Israel-based Memic Innovative Surgery changed its name to Momentis Surgical
- August: MicroPort Navibot announced it received FDA clearance for a robotically assisted total knee replacement solution with its SkyWalker system
    - This is the company's first robot-assisted platform for orthopedic applications, which has the capability of equipping surgeons with information to help achieve the desired joint line reconstruction during a patient's surgery, while also providing data to optimally balance soft tissues
- September: Titan Medical and Medtronic announced in September a limited development program
    - The definitive agreement includes a preclinical collaboration to evaluate the performance of various instruments and cameras in gynecological procedures
- September: Virtuoso Surgical announced it was pursuing a "[Fourth] lane on the surgical robotics highway," bolstered by a $20 million stock offering
    - This new lane of rigid endoscopy will complement the three existing lanes of multi-port, single-port, and flexible laparoscopy
- September: Japan's Ministry of Health, Labour and Welfare announced clearance of da Vinci SP platform from Intuitive Surgical's use in general surgeries, thoracic surgeries

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(excluding cardiac procedures and intercostal approaches), urologic surgeries, gynecological surgeries, and transoral head and neck surgeries
- October: Sunnyvale, CA-based company reported that 3Q22 revenue increased 11% compared to 3Q21
    - The higher third quarter revenue was driven by growth in da Vinci procedure volume, partially offset by a decline in system placements, and that supply chain challenges were subsiding
- October: Medtronic announced in October three significant regulatory milestones for Hugo in Europe, North America, and Asia
    - CE mark clearance to market Hugo for general surgery in Europe
    - A Health Canada license for general laparoscopic surgery
    - MHLW approval for urologic surgical and gynecologic laparoscopic indications in Japan
- Medtronic noted that general surgery is the fastest growing segment within robotic surgery and that Japan is the third-largest robotic surgery market in the world today
- October: Think Surgical of Freemont, CA, also announced in October that it raised $100 million from KDB Investment Global Healthcare of Korea to accelerate the commercial launch of several new products across multiple robotic systems in orthopedics, plus a choice of implants from different manufacturers
- December: Vicarious Surgical will showcase its surgical robotic system at an investor and analyst event in December
    - The platform combines human-like arms with virtual reality technology for minimally invasive abdominal surgery

**Pfizer's hemophilia B gene therapy** - December 29, 2022
https://www.fiercebiotech.com/biotech/pfizers-hemophilia-b-gene-therapy-better-standard-care-phase-3-trial?itm_source=parsely-api
- Pfizer is developing a one-time gene therapy treatment to help patients with hemophilia B develop the Factor IX protein needed to clot blood
    - The current standard of care for these patients is a recurrent Factor IX regimen to prevent and control bleeding
    - The goal of this investigational treatment for people living with hemophilia B, once treated, is that they will be able to produce FIX themselves via this one-time treatment rather than having to receive exogenous FIX
- Pfizer's gene therapy for severe hemophilia B has not only matched standard of care but beat it in a phase 3 study testing whether the treatment can help patients make the protein responsible for blood clotting on their own
- Fidanacogene elaparvovec, which Pfizer licensed from Spark Therapeutics, was being tested in the late-stage trial with 45 male patients who have moderately severe or severe hemophilia B
    - Fidanacogene elaparvovec is a novel, investigational gene therapy that contains a bio-engineered AAV capsid and a high-activity human coagulation FIX gene

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- In the Phase 3 BENEGENE-2 study, Pfizer's gene therapy demonstrated noninferiority and superiority in annualized bleeding rate of total bleeds compared to the standard of care
    - Upon entering the trial, patients received routine treatment and monitoring for six months before receiving a single dose of fidanacogene elaparvovec
    - Patients receiving the gene therapy had 1.3 bleeds between Week 12 after treatment and Month 15, compared to a bleed rate of 4.43 during the six-month monitoring period prior to receiving the medicine
    - That means the gene therapy led to a 71% reduction in the annualized bleeding rate after a single dose
    - Patients taking fidanacogene elaparvovec also had a 78% reduction in treated annualized bleeding rate and a 92% reduction in annualized infusion rate
    - The gene therapy was generally well tolerated; however, there were 14 serious adverse events in seven patients
    - Two of those adverse events, a stomach ulcer bleed and liver enzyme elevations, were considered related to treatment
    - No deaths or serious adverse events associated with infusion were reported
- The FDA has granted the gene therapy breakthrough, regenerative medicines advance therapy and orphan drug designations
- The European Medicines Agency has tagged the gene therapy with Priority Medicines (PRIME) and orphan drug designations
- Pfizer currently has three Phase 3 programs investigating gene therapy in populations where there is a a high unmet need: hemophilia B, hemophilia A, and Duchenne muscular dystrophy
    - The Phase 3 AFFINE (NCT04370054) study is an open-label, multicenter, single arm study to evaluate the efficacy and safety of a single infusion of giroctocogene fitelparvovec in more than 60 adult (ages 18-64 years) male participants with moderately severe to severe hemophilia A
    - Eligible study participants will have completed at least six months of routine FVIII prophylaxis therapy during the lead-in Phase 3 study (NCT03587116) in order to collect pretreatment data for efficacy and selected safety parameters
    - In September 2022, Pfizer and Sangamo Therapeutics announced that the Phase 3 AFFINE study evaluating giroctocogene fitelparvovec, an investigational gene therapy for patients with moderately severe to severe hemophilia A has re-opened recruitment
    - All trial sites will be activate by the end of 2022 and a pivotal readout is expected in the first half of 2024
- A Phase 3 trial is also ongoing investigating marstacimab, a potential novel subcutaneous therapy option being studied for the treatment of people with hemophilia A and B with and without inhibitors
    - https://www.pfizerclinicaltrials.com/find-a-trial/nct05611801-hemophilia-trial
    - In November, Pfizer announced that they plan a phase III BASIS kids trial for hemophilia in adolescents, children and infants

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- The purpose of this clinical trial is to learn about the safety and effects of marstacimab for the patients treatment of hemophilia in paediatric patients
- All participants in this study will receive marstacimab to use prophylactically
- Marstacimab will be given once a week as a subcutaneous (under the skin) shot
- During the 12-month treatment period, weekly doses of marstacimab can be given at home, or if preferred, the doses may be given by the study site staff
- Participants will be in this study for about 14 months (approximately 1 month in a Screening period, 12 months receiving treatment, and 1 month in a follow-up period) during which they will visit the study site at least 10 times

**AbbVie and Immunome Announce Strategic Collaboration to Discover Multiple Novel Oncology Targets** - January 6, 2023
https://news.abbvie.com/article_display.cfm?article_id=12547

- Immunome, Inc. is a clinical-stage biopharmaceutical company that utilizes its human memory B cell platform to discover and develop first-in-class antibody therapeutics
    - Immunome's proprietary Discovery Engine identifies novel therapeutic antibodies and their targets by leveraging memory B cells, highly educated components of the immune system, isolated from patients
    - Memory B cells are key elements in the human immune system response to disease as they produce specific, high-affinity antibodies that bind to cancer antigens or pathogens
    - Immunome's Discovery Engine incorporates high-throughput screening to enable efficient, unbiased, broad, and deep functional evaluation of patient memory B cell repertoires to identify antibodies directed at novel targets
- AbbVie and Immunome announced a worldwide collaboration and option agreement directed to the discovery of up to 10 novel antibody-target pairs arising from three specified tumor types using Immunome's Discovery Engine
- Under the terms of the agreement, Immunome will grant AbbVie the option to purchase worldwide rights for up to 10 novel target-antibody pairs arising from the selected tumors
- Immunome will receive an upfront payment of $30M and will be eligible to receive additional platform access payments in the aggregate amount of up to $70M based on AbbVie's election for Immunome to continue research using its Discovery Engine
- Immunome is also eligible to receive development and first commercial sale milestones of up to $120M per target with respect to certain products derived from target-antibody pairs that AbbVie elects to purchase, with potential for further sales-based milestones as well as tiered royalties on global sales
- This collaboration represents AbbVie's commitment to developing and commercializing novel treatment approaches for solid tumors to enhance their existing oncology pipeline

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**BioNTech signs a deal with the UK government to deliver cancer therapies** - January 6, 2022
https://www.fiercebiotech.com/biotech/biontech-signs-uk-government-pact-deliver-cancer-therapies-100k-patients-2023

- BioNTech has struck a deal with the U.K. government to recruit patients for trials of their cancer immunotherapies
- This collaboration with extend to infectious disease vaccines and BioNTech will invest in both a research hub in Cambridge, England and a regional headquarters in London
- BioNTech intends to make the most of the UK's well-regarded clinical trial network, genomics and national health data resources
- The next steps will be the selection of candidates, trial sites and the set-up of a development plan with the goal of enrolling the first cancer patients in the second half of 2023

**MRD is accelerating effective use of biologic therapies** - January 9, 2023
https://www.fiercebiotech.com/sponsored/how-mrd-accelerating-effective-use-biologic-therapies?itm_source=parsely-api

- Molecular residual disease (MRD) has grown in importance as an oncological biomarker
- The use of tumor-informed liquid biopsy has proven effective in early detection of circulating tumor-derived DNA (ctDNA) indicative of cancer recurrence
- Standard-of-care radiological-based technologies, including CT, PET, and MRI scans, are limited in their ability to detect MRD due to the minimum tumor volume required
- Reliable, ultra-sensitive detection and quantification of MRD capable of guiding clinical decisions from the earliest stages reminds a goal
- To fill the gap, an industry-leading ctDNA technology has evolved to achieve a sensitivity in the range of 1-3 parts per million, representing a 10-100X increase over other available methods, while requiring only a single tube of blood and 1mm of tumor tissue
    - At this level of sensitivity, ctDNA holds great potential both in drug development and as a clinical tool
    - When paired with next generation genomic sequencing, this breakthrough technology - NeXT Personal - enables early identification of cancer mutations to rapidly assess therapeutic effect and inform post-resection therapy
- NeXT Personal enables detection and quantification of both MRD and clinically-relevant variants in a single platform

Detecting ESR1 mutation resistance to aromatase inhibitors

- Aromatase inhibitors are a class of drugs used in the treatment of breast cancer
- Tumors can become resistant to aromatase inhibitors through mutations of Estrogen Receptor alpha (ESR1), which are frequent during disease progression on aromatase-based first-line therapyPADA-1 was the first trial to demonstrate that ESR1 mutations can be detected and targeted before disease progression

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- After detecting the mutations in cell-free DNA, the team initiated a therapeutic switch from an aromatase inhibitor plus palbociclib to Fulvestrant and palbociclib
- This switch resulted in doubled progression-free survival in the phase III PADA-1 trial
- Switching the therapy after disease progression resulted in a minor benefit
- While Fulvestrant is unaffected by the ESR1 mutations, it did provide limited progression-free survival when used as a second-line therapy, highlighting the importance of detecting ESR1 mutations during first-line aromatase therapy and before disease progression
- ctDNA assessment using tumor-informed whole genome sequencing-based and fixed guideline-driven panels in a single assay provides unprecedented insights and facilitates longitudinal therapy response analysis, including variant tracking and proactive monitoring of resistance mechanisms

Predicting clinical outcomes sooner with MRD

- Neoantigens derived from tumor-specific mutations are promising immunotherapy targets that can be incorporated in personalized therapeutic cancer vaccines (PTCV) to boost T-cell activation
- Findings were presented at the Society for Immunotherapy of Cancer 37th Annual Meeting illustrating the correlation of disease status with ctDNA levels relative to baseline
- Researchers treated patients with unresectable or metastatic hepatocellular carcinoma that were non-responsive to first-line tyrosine kinase inhibitor therapy, with PTCV and observed a strong correlation between ctDNA quantification and tumor size over 2 years
- Importantly, changes in ctDNA measured prior to MRI scans and RECIST 1.1. analysis were directly associated with objective clinical response such as overall survival, with no false-negatives reported
- These results show that longitudinal high-sensitivity ctDNA monitoring could help predict clinical outcome and guide real time clinical treatment decisions for personalized cancer therapy
- Ease of ctDNA sample handling and analysis, along with rapidly accessible MRD data offer significant advantages for fast and effective drug development
- The value of longitudinal ctDNA measurement as a dynamic biomarker for treatment response prediction, understanding of emergent tumor variants and real time clinical treatment decision-making is supported by a growing body of evidence