New Health - models for success using AI and Digital Therapeutics

Dr. Michael C. Müller

Bünde, September 14th, 2020

Industry today

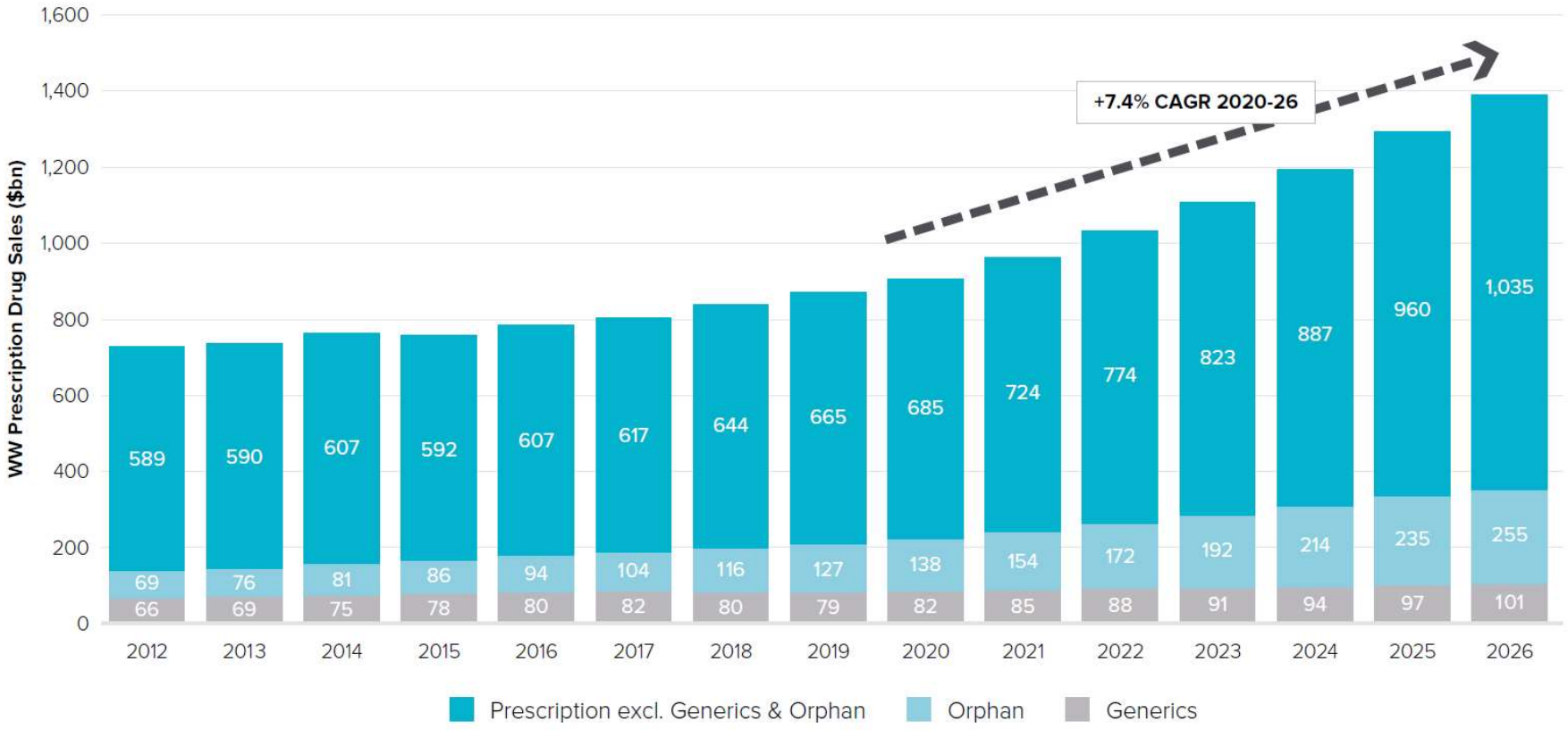
A steadily growing world-population, increasing disease prevalence and population aging, are driving healthcare costs massively

- **By 2050**, the **world population is projected to be almost 10 billion people -** strongest growth is expected to occur in **Africa**
- **Total global health** spending will be around **$15.0 trillion by 2050**
- **By then**, most **OECD countries** will spend more than **20% of their GDP** on healthcare
- The **US** will have to devote almost **40%** of GDP to healthcare until 2050
- In this context, countries like **China and India will increase their overall share of total health expenditure to almost 20%**

Source: Rheumatology Advisor; Statista

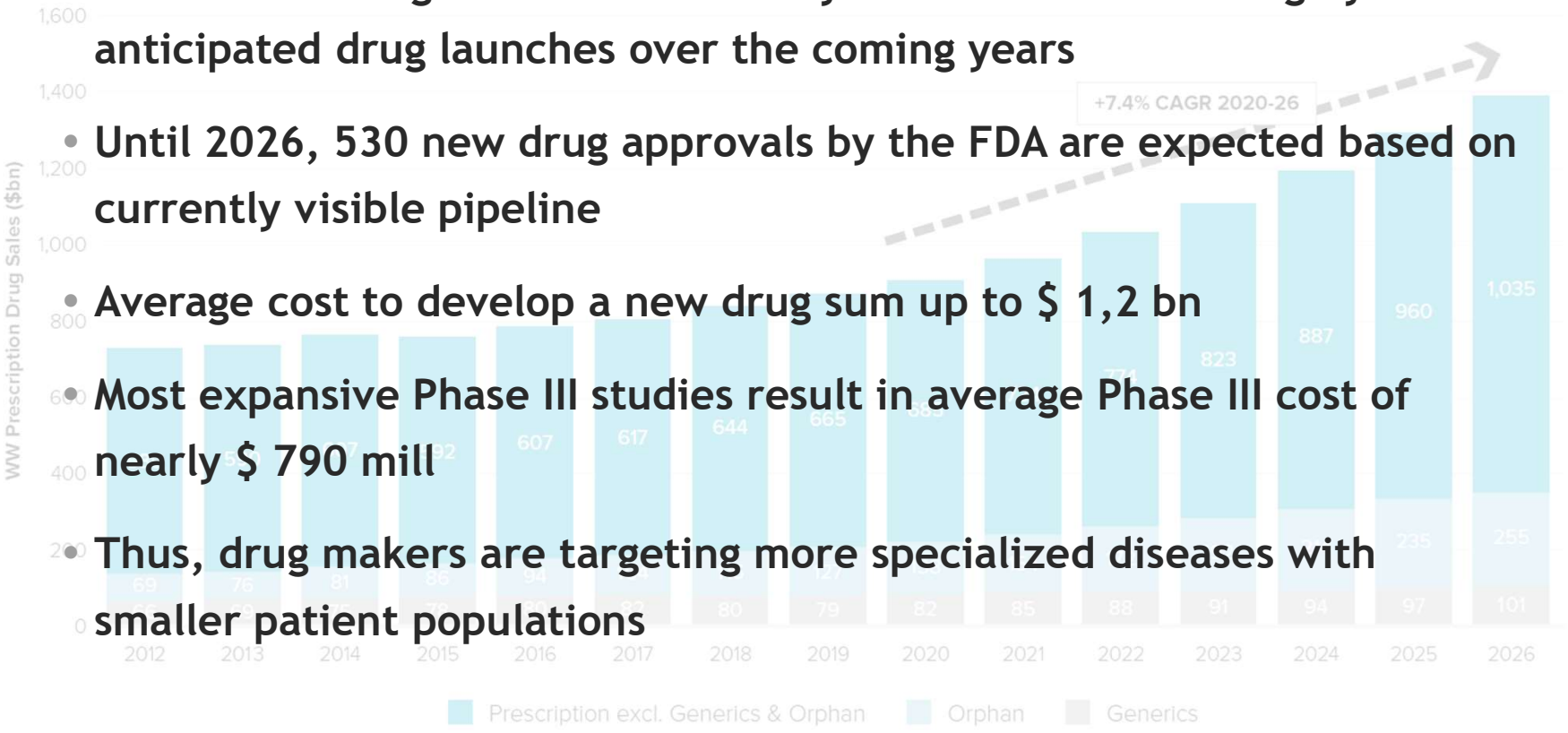
Prescription drug sales will further grow by >7% p.a. reaching 1,4 trillion already by 2026

Worldwide Total Prescription Drug Sales (2012-2026)



Source: EvaluatePharma® World Preview 2020

- The forecasted growth can be mostly attributed to some highly anticipated drug launches over the coming years
- Until 2026, 530 new drug approvals by the FDA are expected based on currently visible pipeline
- Average cost to develop a new drug sum up to $ 1,2 bn
- Most expansive Phase III studies result in average Phase III cost of nearly $ 790 mill
- Thus, drug makers are targeting more specialized diseases with smaller patient populations



Source: EvaluatePharma® World Preview 2020

Growth will mainly be driven by few therapeutic classes

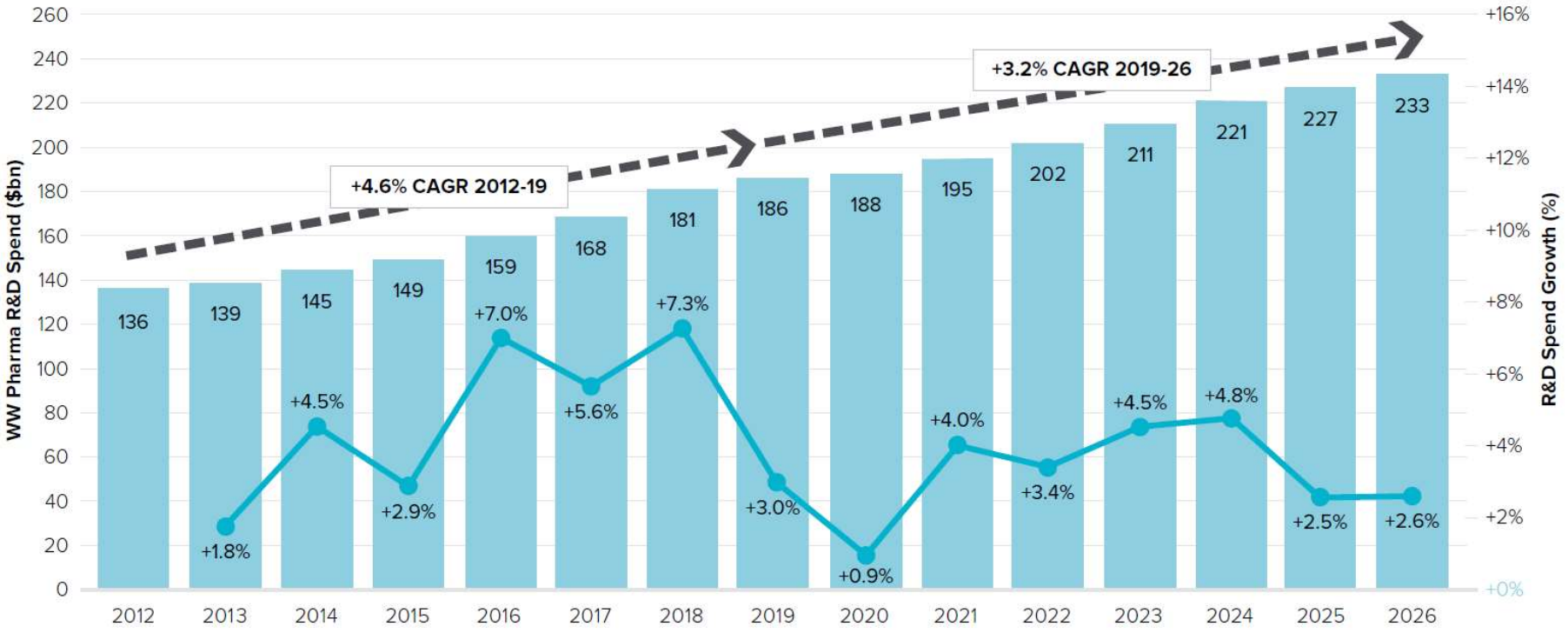
Worldwide Prescription Drug & OTC Sales by Evaluate Therapy Area (2019 & 2026): Top 15 Categories & Total Market

Rank	Therapy Area	WW Sales ($bn) 2019	WW Sales ($bn) 2026	CAGR % Growth	WW Market Share 2019	WW Market Share 2026	Chg. (+/-)	Rank Chg. (+/-)
1.	Oncology	145.4	311.2	+11.5%	16.0%	21.7%	+5.8pp	+0
2.	Anti-diabetics	51.0	66.9	+3.9%	5.6%	4.7%	-0.9pp	+1
3.	Immunosuppressants	24.0	61.3	+14.3%	2.6%	4.3%	+1.6pp	+4
4.	Vaccines	32.5	56.1	+8.1%	3.6%	3.9%	+0.3pp	+1
5.	Anti-rheumatics	56.9	49.7	-1.9%	6.3%	3.5%	-2.8pp	-3
6.	Anti-virals	38.8	42.9	+1.5%	4.3%	3.0%	-1.3pp	-2
7.	Sensory Organs	23.8	35.1	+5.7%	2.6%	2.4%	-0.2pp	+1
8.	Bronchodilators	27.8	32.2	+2.1%	3.1%	2.3%	-0.8pp	-2
9.	Dermatologicals	13.8	32.0	+12.7%	1.5%	2.2%	+0.7pp	+3
10.	MS therapies	22.7	25.0	+1.4%	2.5%	1.7%	-0.7pp	+0
11.	Anti-hypertensives	23.4	22.4	-0.6%	2.6%	1.6%	-1.0pp	-2
12.	Anti-coagulants	21.3	22.0	+0.5%	2.3%	1.5%	-0.8pp	-1
13.	Anti-psychotics	11.2	21.0	+9.5%	1.2%	1.5%	+0.2pp	+2
14.	Anti-fibrinolytics	13.4	19.7	+5.7%	1.5%	1.4%	-0.1pp	-1
15.	Sera & gammaglobulins	11.5	19.5	+7.8%	1.3%	1.4%	+0.1pp	-1
	Top 15	517.5	816.9	+6.7%	56.9%	57.1%	+0.2pp	
	Other	392.5	614.6	+6.6%	43.1%	42.9%	-0.2pp	
	Total WW Prescription & OTC Sales	**910.0**	**1,431.5**	+6.7%	100.0%	100.0%		
	Total 'Prescription & OTC Sales' includes:							
	WW Generic Sales	**79.5**	**100.7**	+3.4%	8.7%	7.0%	-1.7%	
	OTC Pharmaceuticals	**38.3**	**41.4**	+1.1%	4.2%	2.9%	-1.3%	

Source: EvaluatePharma® World Preview 2020

Also worldwide pharmaceutical R&D spend is forecasted to grow steadily at a CAGR of 3.2% reaching $232.5bn in 2026

Worldwide Total Pharmaceutical R&D Spend in 2012-2026



Source: EvaluatePharma® World Preview 2020

Keytruda will continue to dominate sales to become the top selling drug in the world in 2026 with sales of $24.9bn

Rank	Product	Generic Name	Company	Route of Administration	Mechanism of Action	2019	2026	CAGR	Indication
1.	**Keytruda**	pembrolizumab	Merck & Co	intravenous	Programmed cell death protein 1 antibody	11,121	24,910	12.2%	Tumor
2.	**Opdivo**	nivolumab	Bristol-Myers Squibb	intravenous	Programmed cell death protein 1 antibody	7,989	12,677	6.8%	Tumor
3.	**Eliquis**	apixaban	Bristol-Myers Squibb	oral	Coagulation factor Xa inhibitor	7,929	12,551	6.8%	Thrombosis/ Stroke
4.	**Biktarvy**	bictegravir sodium; emtricitabine; tenofovir alafenamide fumarate	Gilead	oral	HIV-1 integrase inhibitor; HIV-1 nucleoside reverse transcriptase inhibitor	4,378	11,711	13.8%	Tumor
5.	**Imbruvica**	ibrutinib	AbbVie	oral	Bruton's tyrosine kinase inhibitor	5,686	10,722	9.5%	HIV-1 infections
6.	**Ibrance**	palbociclib	Pfizer	oral	Cyclin-dependent kinase 4 inhibitor;Cyclin-dependent kinase 6 inhibitor	4,961	9,683	10.0%	Breast cancer
7.	**Tagrisso**	osimertinib mesylate	AZ	oral	Epidermal growth factor receptor inhibitor	3,189	9,514	16.9%	Tumor
8.	**Dupixent**	dupilumab	Sanofi	subcutaneous	Interleukin-13 antibody; Interleukin-4 antibody	2,322	9,386	22.1%	Leukemia/Mantle cell lymphoma
9.	**Trikafta**	elexacaftor; ivacaftor; Tezacaftor	Vertex Pharma.	oral	Cystic fibrosis transmembrane conductance regulator potentiator; Cystic fibrosis transmembrane conductance regulator	420	8,739	54.3%	Cystic fibrosis
10.	**Ozempic**	semaglutide	Novo Nordisk	subcutaneous	Glucagon-like peptide 1 receptor agonist	1,685	8,321	25.6%	Type 2 diabetes

Source: EvaluatePharma® World Preview 2020

Eli Lilly's anti-diabetic and obesity drug is the most valuable project with an NPV of $7.8bn

Top 10 Most Valuable R&D Projects (Ranked by Net Present Value)

Rank	Product	Company	Route of Administration	Mechanism of Action	Today's NPV ($m)	Indication
1.	**Tirzepatide**	Eli Lilly	subcutaneous	GLP-1 receptor agonist	7,832	Obesity/Type 2 diabetes
2.	**Inclisiran**	Novartis	subcutaneous	Proprotein convertase subtilisin/kexin type 9 inhibitor	7.422	Hypercholesterolemia
3.	**Efgartigimod**	argenx	oral	Neonatal Fc receptor antibody	5,650	Myasthenia gravis Idiopathic thrombocytopenic purpura
4.	**BMS-986165**	Bristol-Myers Squibb	oral	Tyrosine kinase 2 inhibitor	5,638	Psoriasis/Crohn's/Psoriatic Arthritis/Ulcerative Colitis
5.	**ALN-HBV02**	Vir Biotechnology	subcutaneous	Hepatitis B polymerase RNAi	5,459	Hepatitis B
6.	**Aducanumab**	Biogen	subcutaneous	Beta amyloid A4 protein antibody	5,5361	Alzheimer's disease
7.	**Belantamab Mafodotin**	GlaxoSmithKline	intravenous	Tumor necrosis factor receptor 17	5,338	Multiple myeloma
8.	**LN-144**	Iovance Biotherapeutics	intravenous	Tumor infiltrating lymphocytes cell therapy	5,162	Malignant melanoma
9.	**AK002**	Allakos	intravenous	Immunoglobulin-type lectins-8 antibody	5,126	Eosinophilic esophagitis/ Gastroenteritis
10.	**Risdiplam**	Roche	oral	Survival motor neuron 2 protein stimulant	5,087	Spinal muscular atrophy
	Top 10				58,076	
	Other				506,663	
	Total				564,738	

Source: EvaluatePharma® World Preview 2020

Eli Lilly's anti-diabetic and obesity drug is the most valuable project with an NPV of $7.8bn

$ 2 bn phase III trial with more than 12.000 patients

Top 10 Most [illegible] sent Value)

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Source: EvaluatePharma® World Preview 2020

The Top 10 labs will see minor changes only in their ranking until 2026

Top 10 Most Valuable R&D Projects (Ranked by Net Present Value)

Rank	Sales ($bn) 2019	Company
1.	48.2	Roche
2.	46.1	Novartis
3.	43.8	Pfizer
4.	40.9	Merck & Co
5.	40.1	Johnson & Johnson
6.	34.9	Sanofi
7.	32.4	AbbVie
8.	31.3	GSK
9.	25.2	Bristol-Meyers Squibb
10.	23.2	AstraZeneca

Company	Sales ($bn) 2026	Rank
Roche	61	1.
Johnson & Johnson	56.1	2.
Novartis	54.8	3.
Merck & Co	53.2	4.
AbbVie	52.7	5.
Pfizer	51.1	6.
Bristol-Meyers Squibb	44.7	7.
Sanofi	41.7	8.
AstraZeneca	41	9.
GSK	40.8	10.

Source: EvaluatePharma® World Preview 2020

Diabetes will be the major cost burden for worldwide healthcare systems

- **By 2030,** the estimated number of people living with Diabetes will **exceed 570 million**. Around **450 million people** of this estimation will be living in a middle-income situation

- **India** will have to treat **~100 million people** with **diabetes** and **China** will top the list with an estimated **140 million Diabetes patients** by **2030** (today 9.5 million in Germany)

- Consequently, the **global cost of diabetes** is set to almost double to **2.5 trillion € in 2030**

Source: Evaluate Pharma

Only a few other indications will drive the overall market growth bringing huge demand for pens and other innovative injector technologies

- Many fast growing markets refer to unmet needs within the group of so called **"immunological or autoimmune"** diseases
- The **Rheumatoid Arthritis** (RA) market is expected to grow above average bringing fresh demand in mature markets (US, France, Germany, Italy, Spain, the UK, Japan, and Australia)
- **125 million** people worldwide – 2% to 3% of the total population – suffer from **Psoriasis**
- The market for **Psoriasis Treatment** was valued $ 18.4 bn **in 2018** expected to bouble until 2026 reaching **$ 37.6 bn**
- In that period the **Multiple Sclerosos** market will grow from **$19.8bn to $32.9bn** due to the launch of 11 new pipeline agents providing more options for patients
- The **Inflammatory Bowel** disease treatment market is anticipated to reach **USD 22.4 billion by 2026**, exhibiting a CAGR of 4.4% from 2018 to 2026
- **Crohn's disease** dominated the market by type in 2018 but **Ulcerative Colitis** estimated to be the fastest growing segment

Source: Evaluate Pharma

Source: Imcyse

Plenty of innovative Diabetes therapies in sight - however, commercial relevance as for now still low

Overview on companies with innovative treatment approaches

Diabetes Type 1

Cell therapy

Orgenesis™ · ViaCyte · Biocapan · Diabetes Research Institute Foundation – The Best Hope for a Cure®

Immunotherapy

Imcyse – specific active immunotherapeutics · ACT[]BIO THERAPEUTICS™

Artificial pancreas

Dexcom – Continuous Glucose Monitoring · diabeloop · EOFLOW · Medtronic

Diabetes Type 2

Stimulation of insulin production

poxel · Betagenon · morphosys

Targeting the microbiome

Caelus Health · Vedanta Biosciences · Rebiotix – Microbiota Restoration Therapy – A Ferring Company

Source: stradoo

Over the last couple of years, the biotech started to strive to develop new diabetes treatments and to ultimately chasing the holy grail: a cure

Overview on innovative treatment approaches

Diabetes Type 1

01| Cell therapy

- **Cell-based** therapies are aimed at producing functional insulin-secreting ß-cells to restore the body's ability to regulate blood sugar

02| Attacking the origin with immunotherapy

- A further way to cure diabetes type 1 is to **stop the immune system from destroying insulin-producing cells** at an early stage
- Hence, various pharmaceutical manufacturers have developed multiple approaches to preserve these cells

03| Automated treatment with artificial pancreas

- An artificial pancreas depicts an automated system of glycosometer and pumps, which injects insulin based on the current glucose-level of the patient

Diabetes Type 2

01| Stimulating insulin production

- **Poxel** – Insuline effect on Pancreas, Liver, Muscle
- **Morphosys** - MOB in Pen to ruduce fat and insulin resistance
- **Betagenon** (Baltic Bio) – to simultaneously reduce glucose and blood pressure

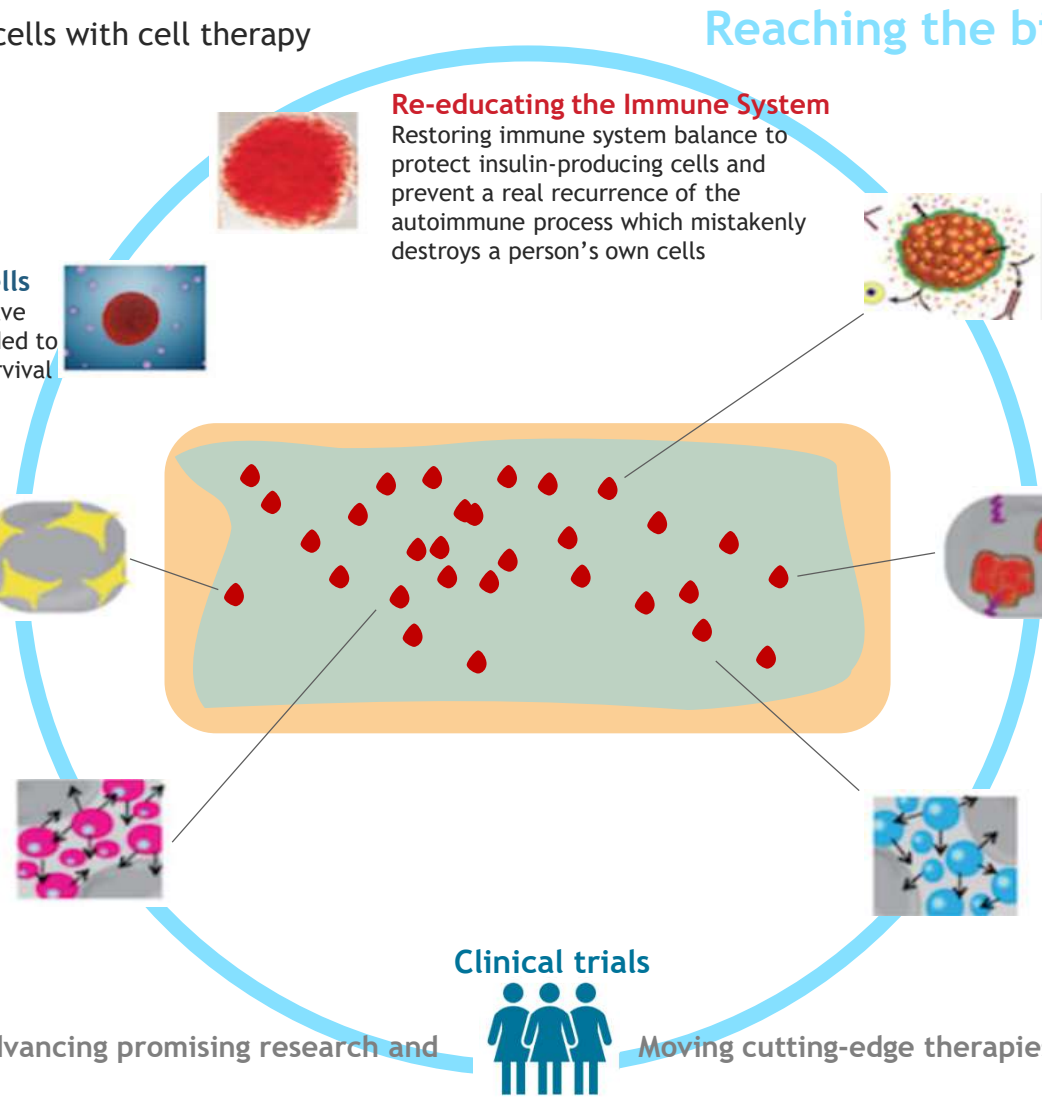
02| Targeting the microbiome

- Research found that patients with diabetes have a **less diverse gut microbiome** as compared to healthy people
- It is shown, that **fecal transplants**, used to transfer the microbiome of healthy person to the gut of one with diabetes, results in short-term **improvement of insulin resistance**

Source: stradoo

Cell-based therapies are aimed at producing functional insulin-secreting ß-cells to restore the body's ability to regulate blood sugar

01 | Replacing missing cells with cell therapy



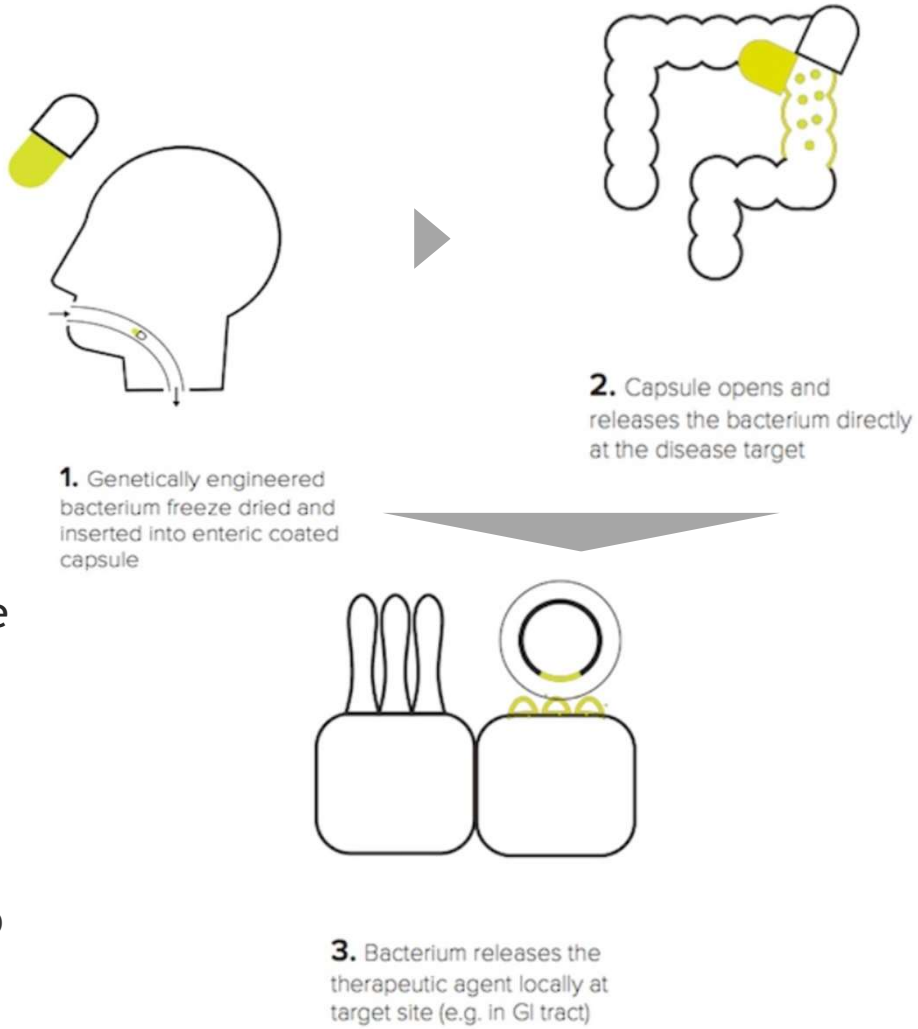
Source: labiotech.eu

Immunotherapy aims to stop the immune system from destroying insulin-producing cells at an early stage

02| Attacking the origin with immunology

ACTBIO THERAPEUTICS™

- **ActoBio** uses a **phase I/II clinical trial** with a new approach to **stop the progression of diabetes**
- The method describes an **oral treatment**, which will be **prescribed for a limited period of time** with the aim to eliminate the need for insulin
- The firm **cheese-producing bacteria** to deliver two drugs **that stimulate regulatory T-cells** to instruct the immune system not to attack insulin-producing cells



Source: ACTBIO

- **The industry is breaking fresh grounds**, turning away from the conventional therapies and the old model of R&D, focusing on collaborations and innovations generated outside the traditional core competences

- **Genome sequencing and personalized medicine** will revolutionize diagnostics, treatment and prevention

- **Digital therapeutics** have become an integral part of diagnose and treatment

- **Artificial intelligence** may provide breakthrough solutions for many unmet needs, for each costumer and for the industry itself

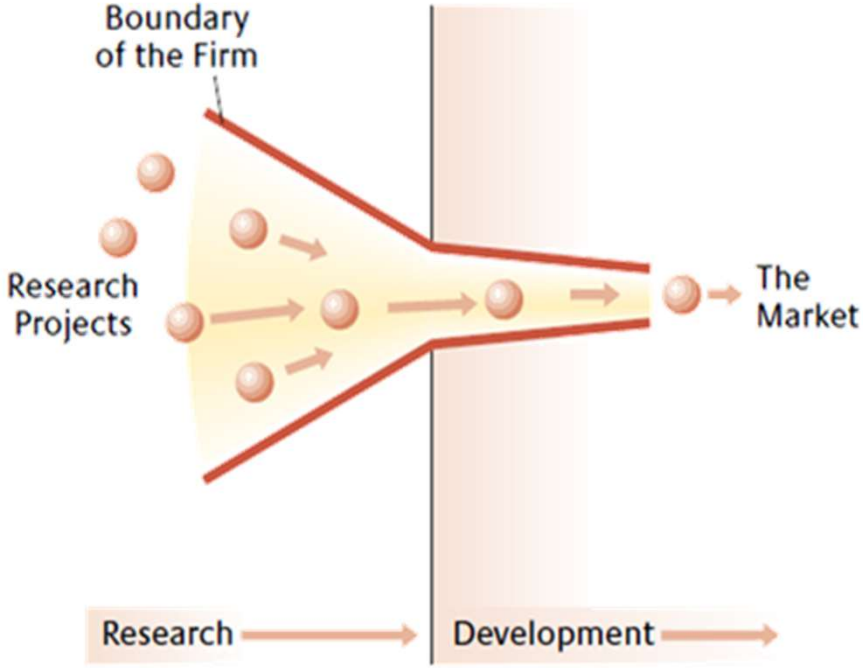
- **Payors will have to adapt** to the new paradigms

The industry is breaking fresh grounds

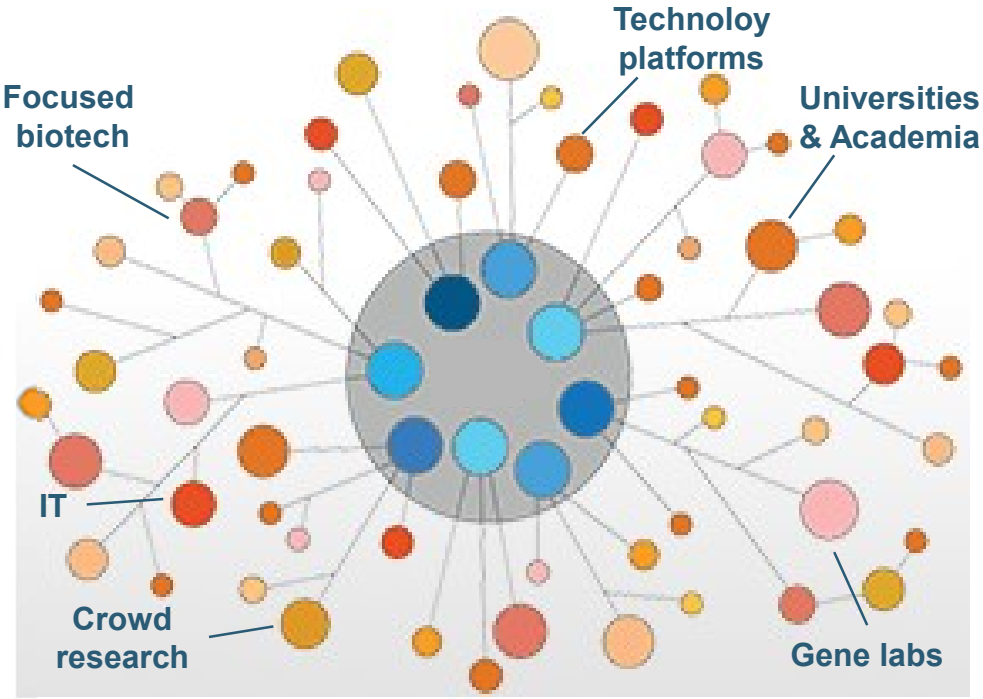
Research will switch from a mono-directional, in-house to a highly collaborative work model

Shift from closed innovation to open innovation in the industry

Yesterday: **Closed innovation**



Tomorrow: **Open innovation**



Source: stradoo

Big Pharma companies are collaborating with other tech-companies in order exploit the great potential of AI

Pharma collaborations/partnerships for AI

- In 2018, **Bayer** announced an **AI** collaboration with **Cyclica** to take its **discovery of peptide drugs to an advanced level**
- Both companies to **discover and design drugs faster**

- **Boehringer Ingelheim** has partnered with UK-based **Bactevo** to **speed up its drug discovery** efforts
- Boehringer will leverage Bactevo´s **AI-powered** platform **TIME** to boost the **efficiency, speed and quality of drug discovery**

- Signed **a $43 M drug discovery collaboration** with **Exscientia** to **identify small molecules** for ten selected targets
- Using rapid **"design-make-test"** cycle **Exscientia** is able to design new molecules using AI-system, employing as **well phenotypic and high content screening data**

Source: press releases

Source: Cyclica

Big Pharma companies are collaborating between them and with other AI tech companies in order exploit the great potential that AI offers (1/2)

Pharma collaborations/partnerships for AI

- **Bayer** takes advantage of **AI** to improve **drug adherence** and **detect potential side effects much earlier**
- **Genpact's AI solution** has been used severally in clinical trials to **change the dosage given to specific patients to optimize the results**

- Abbvie partnered with New York-based **AiCure** to enhance **drug trial vigilance** and **improve drug adherence**
- Abbvie uses **facial and image recognition** algorithm of AiCure **mobile SaaS platform** to **monitor adherence**

- **Naritas** leverages AI and other novel technologies to facilitate the discovery of new and more robust food and healthy ingredients
- BASF uses their **DNA analysis** to **predict, analyze and validate peptides** from natural sources for healthy food (e.g. in diabetes)

Source: Press releases, Healthcare weekly

Big Pharma companies are collaborating between them and with other AI tech companies in order exploit the great potential that AI offers (2/2)

Pharma collaborations/partnerships for AI

AstraZeneca
BERG

- Announced major pharma collaboration with **AstraZeneca on identification and evaluation of novel approaches** for **Parkinson's disease** and other **neurological** disorders
- Uses AI-driven drug discovery to **explore a selection of chemical fragments** provided by **AstraZeneca** to **find promising drug candidates**

Takeda
Numerate

- Takeda is collaborating with the AI-driven **drug design** company Numerate to **develop new clinical candidates** in oncology, gastroenterology, and central nervous system disorders
- Numerate´s AI-platform is able to work with data points obtained from different studies -- from **high-content, low-throughput phenotypic assays** as well as high-throughput **screening**, **structure-based design** and traditional **computational** method

almirall
IKTOS

- In December 2019, **Iktos announced a partnership with Almirall** to use its generative modelling technology **to design novel optimized compounds** and speed identification of **promising drug candidates** for undisclosed indications
- Iktos' AI technology, based on deep generative models, helps bring speed and efficiency to the **drug discovery process**, by automatically designing **virtual novel molecules** that have all **desirable characteristics** of a novel drug candidate

Source: Press releases, Bench Sci

BERG Interrogative Biology uses AI to model complete diseases in silico and develop individual therapies

1) Mimic diseased & healthy environments

In vitro cell cultures

(2) Measure omics over time

Lipids, metabolites, proteins, genes

3) Build the bigger picture

Combine OMIC data with patient clinical information

(4) Process trillions of data using AI: bAIcis®

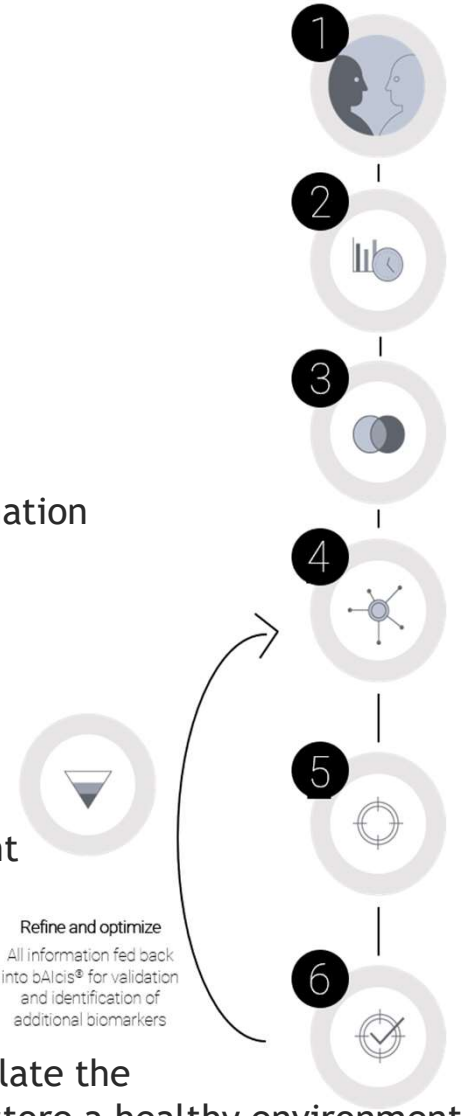
Compares all the data

(5) Derive insights

Map represents the molecules that are abundant or deficient in diseased tissue indicating potential treatments or biomarkers

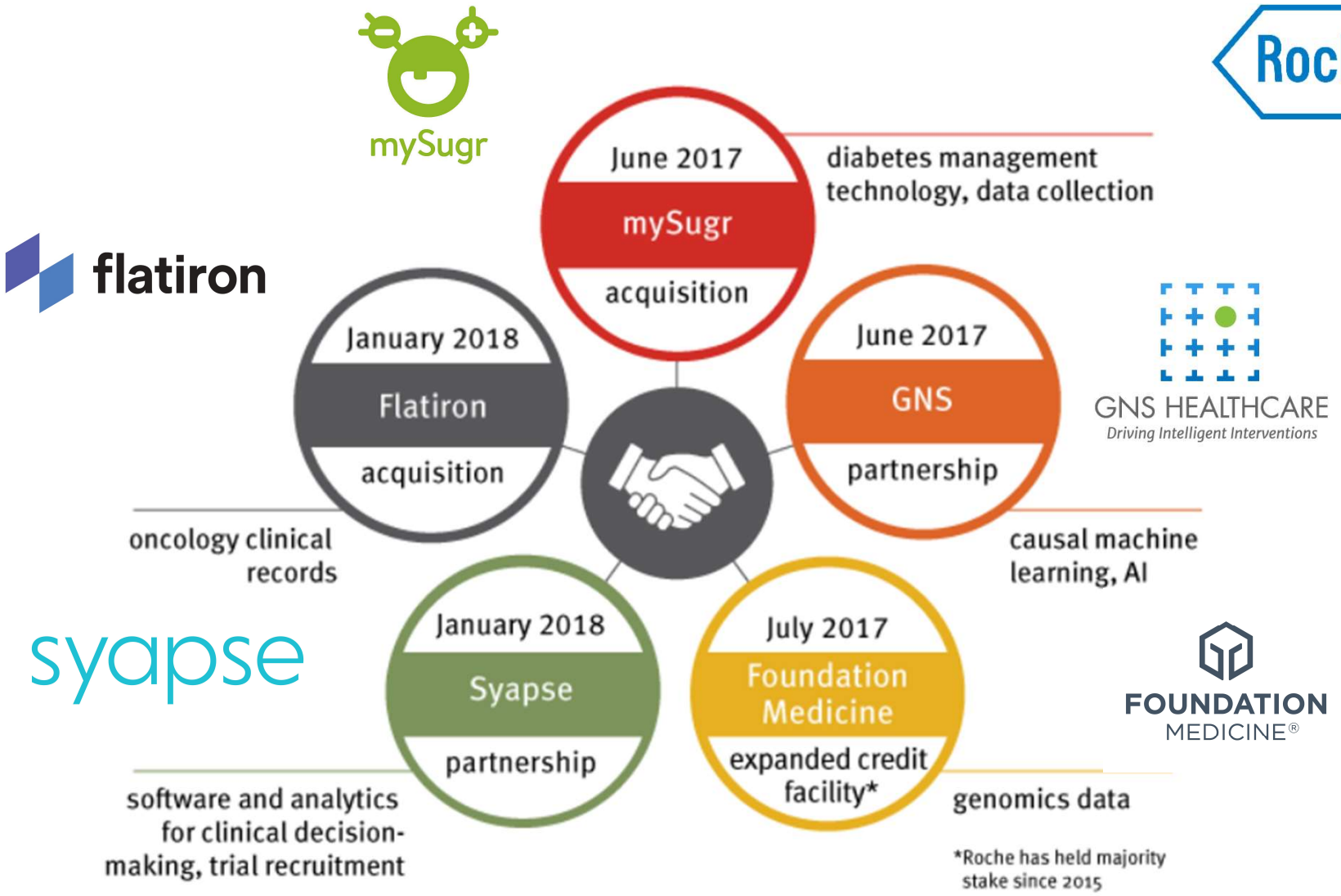
(6) Pressure test

Potential treatments can be created that modulate the target lipids/metabolites/proteins/genes to restore a healthy environment



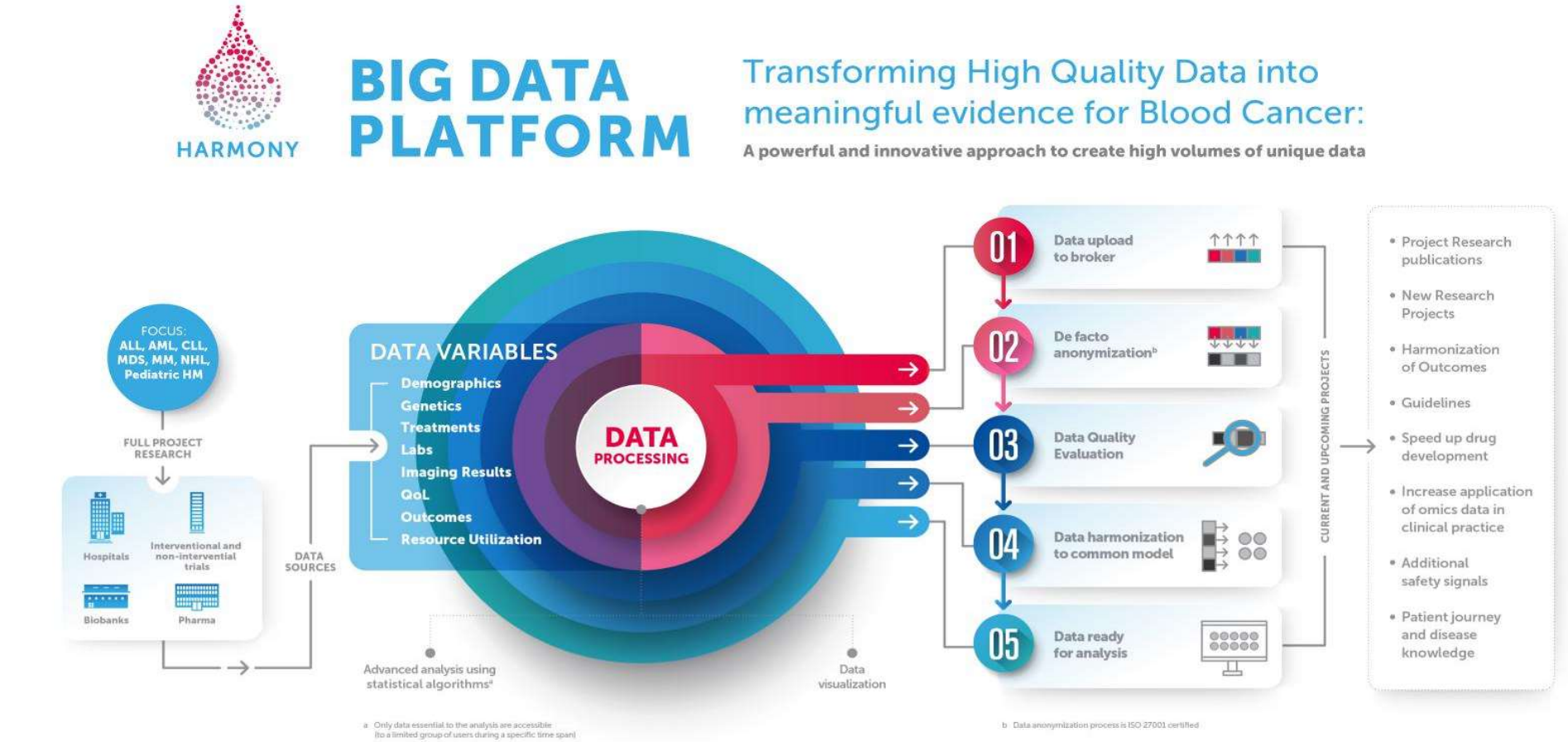
Source: Berghealth

Roche has broken up its value chain collaborating massively with digital solutions



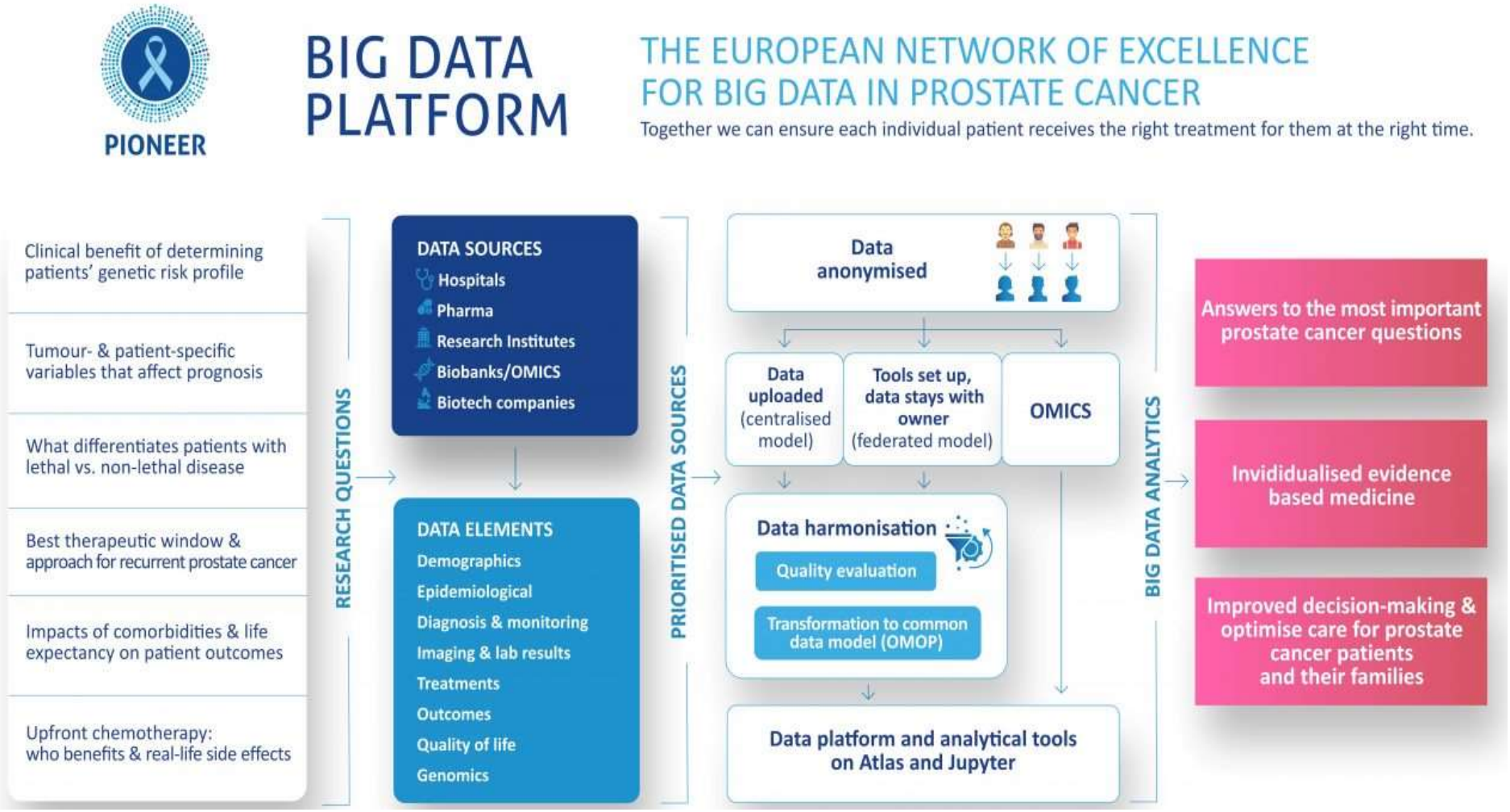
Source: In Vivo, Strategic Transactions, Roche

BigData is combining clinical and genetical information to identify patterns which cannot be seen in conventional clinical trials

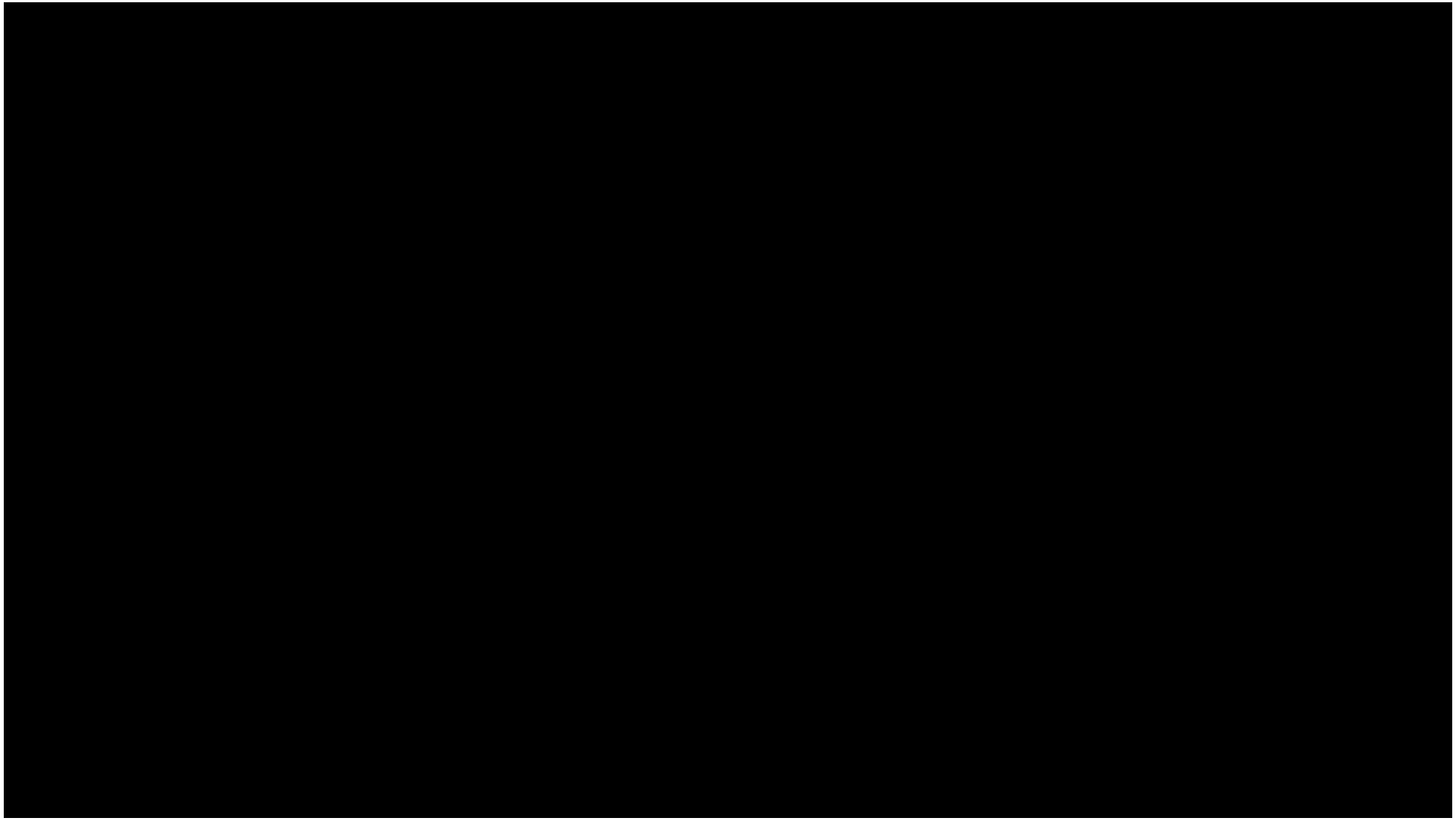


Source: HARMONY

BigData is combining clinical and genetical information to identify patterns which cannot be seen in conventional clinical trials

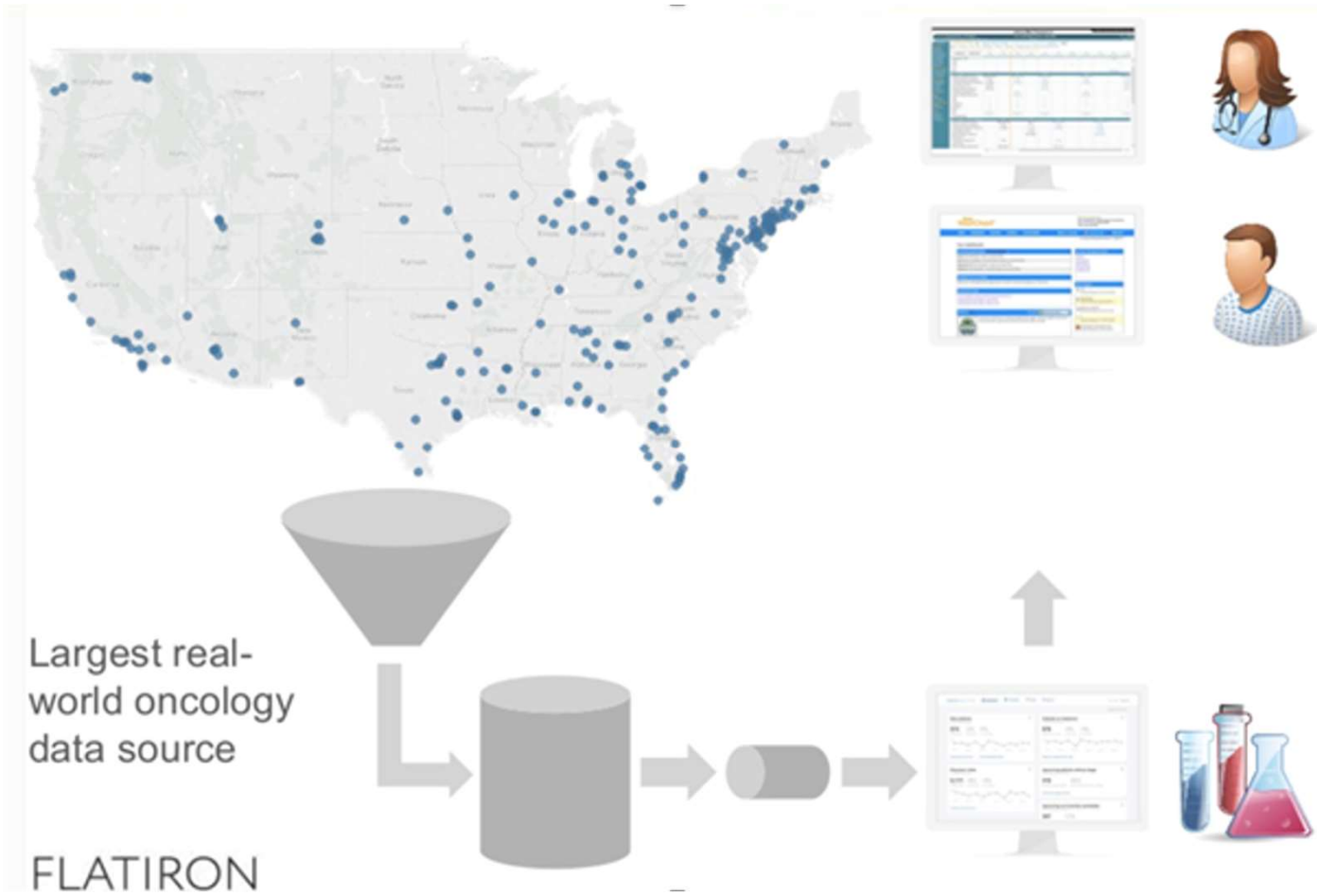


Source: PIONEER



Source: Project Data Sphere

Flatiron Health – aquired by Roche for 1.9 $bn - aggregates data from EHRs for cloud-based for insights to patients, providers and payors



Uses big data analytics to allow providers gaining deep clinical intelligence

Aggregates patient data from EHRs in community oncology practices (hospitals and labs) across the US

OncoTrials makes it easy to quickly **identify and contact potential clinical trial candidates**

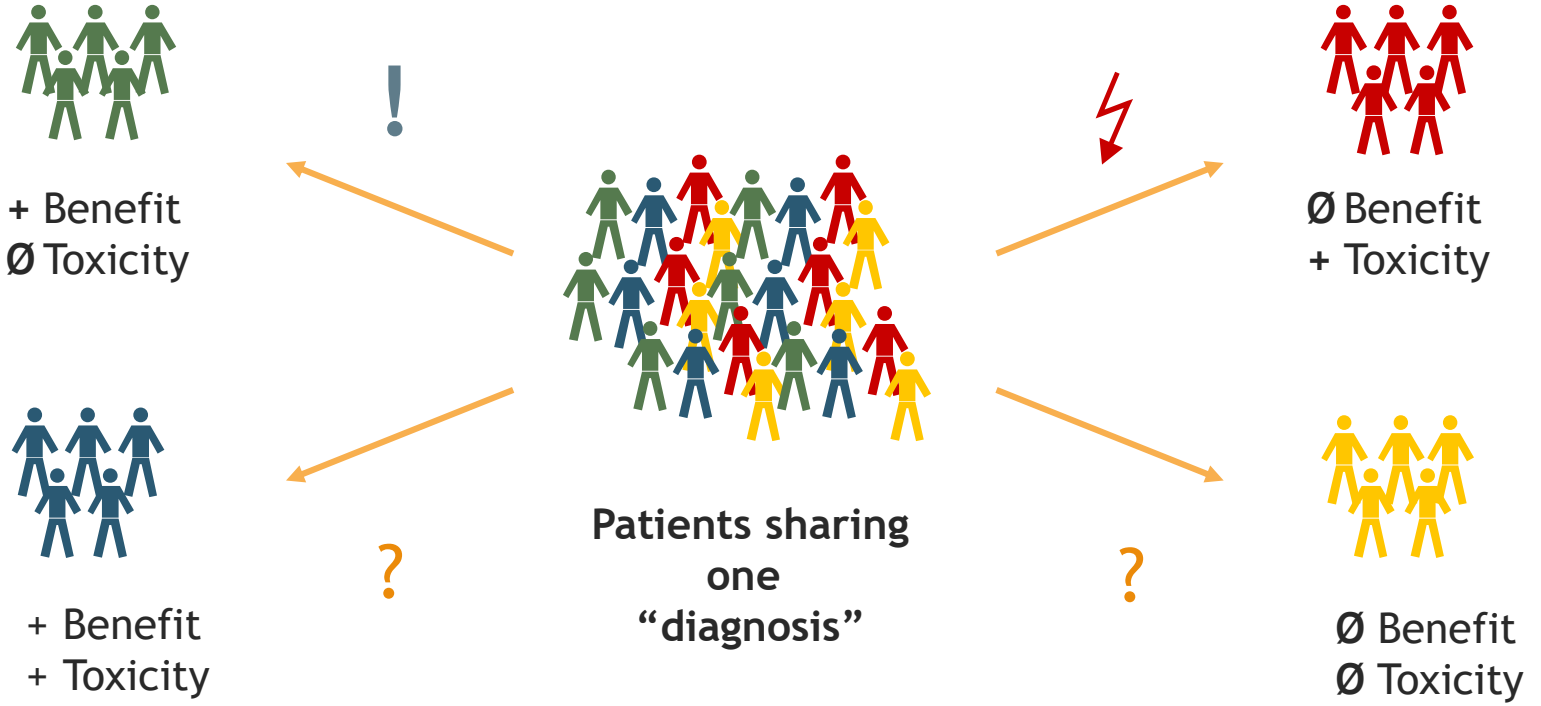
OncologyCloud analyzes the complete **lifecycle of a drug** from administration through to charging and receipt

Source: Flatiron Health, Roche

Genome sequencing and personalized medicine will revolutionize diagnostics, treatment and prevention

Stratified medicine aims to maximize the benefit-risk-ratio of drugs by predicting a better response for a sub-population of patients

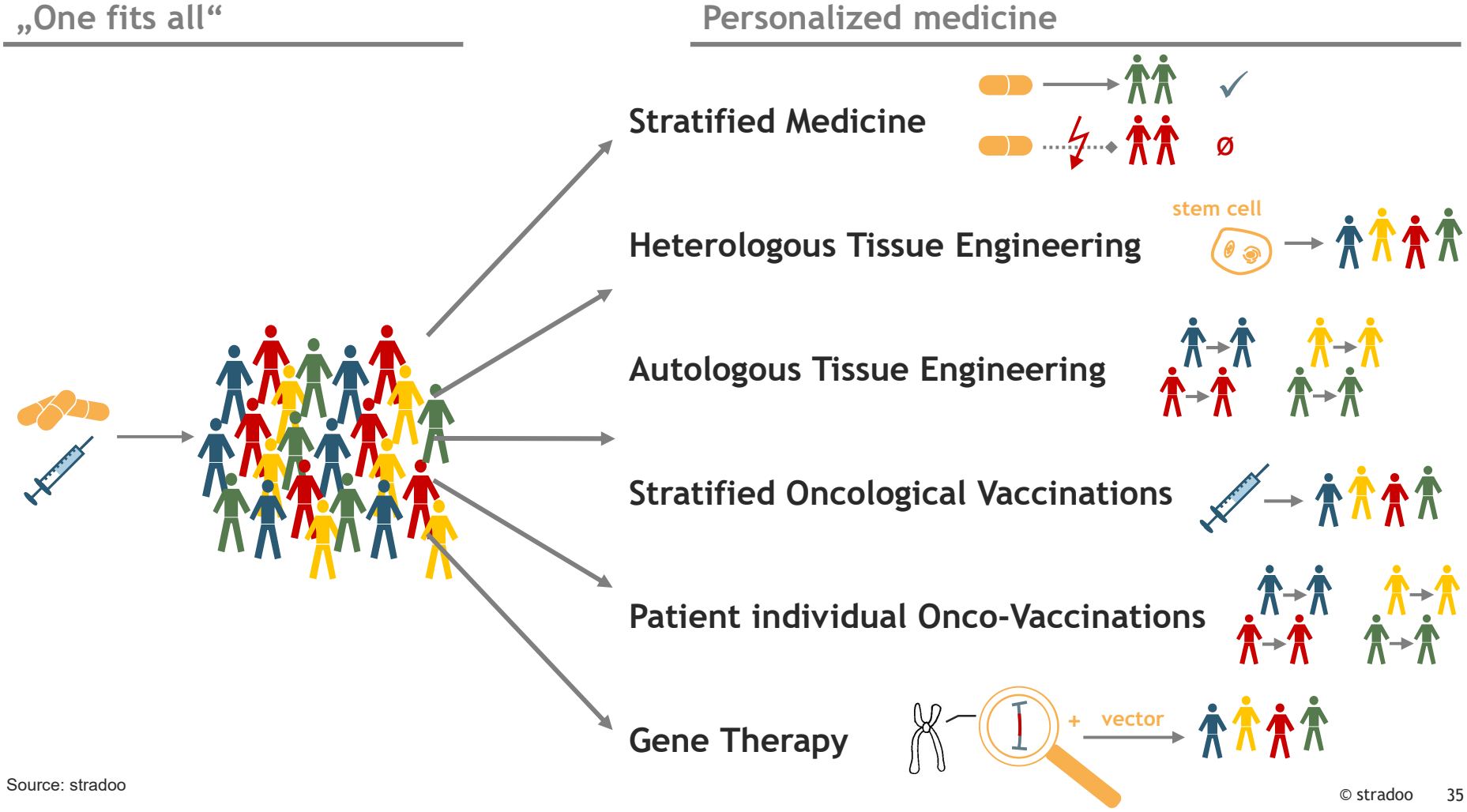
Principle of Stratified Medicine



Source: stradoo

Personalized Medicine represents a drastic departure from the conventional treatment paradigm

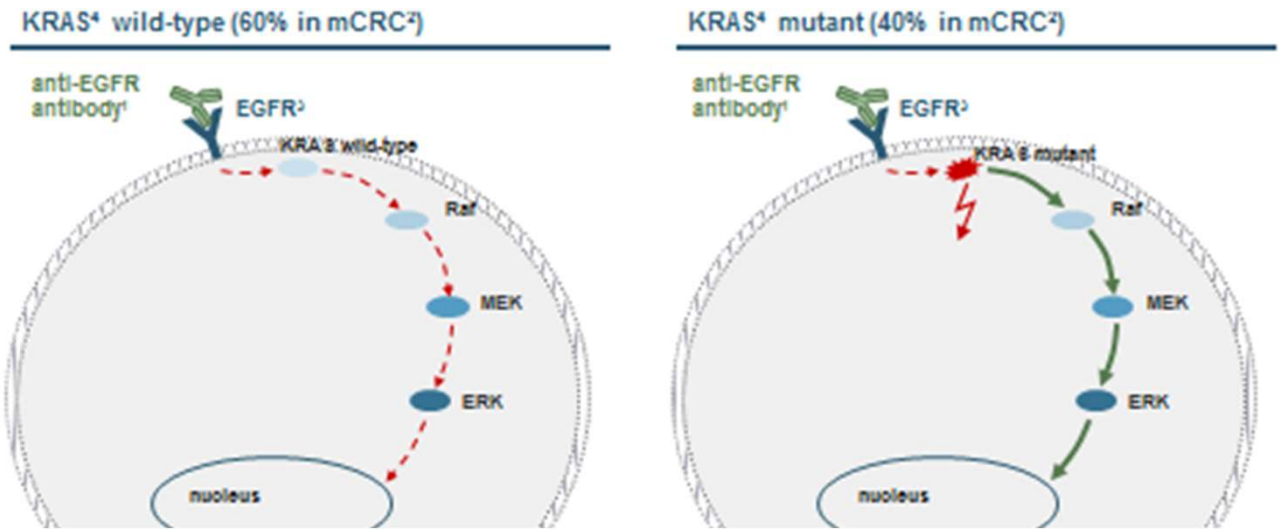
Personalized Medicine – the scope shifts from standardized to highly individualized solutions



Source: stradoo

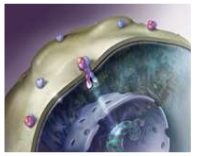
Based on individual mutations, a drug will work in a certain patient or not

Targeted therapies – anti-EGFR therapy[1] and KRAS[4] / HER2+ and Herceptin®

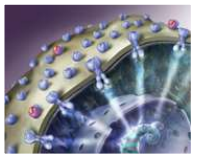


Signal down-regulated due to receptor inhibition by anti-EGFR antibody

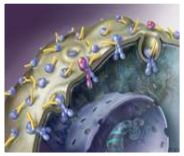
Signal up-regulated due to constitutive KRAS activation



HER2[1] normally expressing cell



HER2 over-expression causing increased cell proliferation



HER2 antibodies binding to receptors thereby inhibiting tumor growth

!

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Roche

1) e.g. Cetuximab or Panitumumab 2) mCRC = metastatic colorectal carcinoma; wildtype KRAS in NSCLC (non-small-cell lung cancer) 80-90% and in head-and-neck cancer 95%
3) EGFR = epidermal growth factor receptor 4) KRAS = Kirsten rat sarcoma 2 viral oncogene homologue, a signaling protein activating among other the MAP-kinase signaling pathway
Source: stradoo

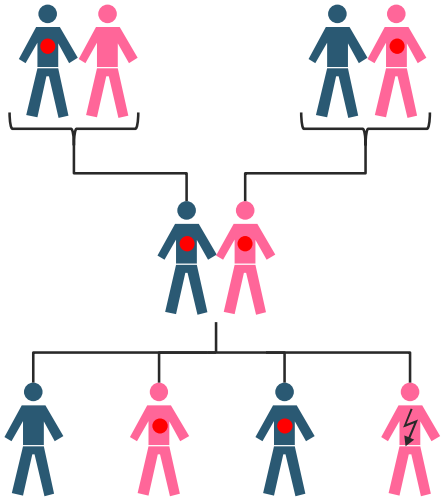
New, ultra-fast genomic sequencing technologies allow to prevent genetic diseases in new-borns before they manifest

Genomic sequencing allows to prevent rare genetic disease Phenylketoneuria

- Phenylketonuria (PKU) causes severe d**amage to nervous system and brain** if undetected (1 in 15,000 newborns positive)

- **Immediate therapy** (with Sapropterin; Kuvan®) after birth is needed to **prevent** disease from **manifesting** as at later stages **no therapy** is possible any more

- New**, fast genomic sequencing** technology allows to run tests within **two days**, quick enough to deliver **prevention** in all cases



PKU is a hereditary disease, yet just **one in four** children of carrier parents develop overt **PKU**

Children's Mercy KANSAS CITY

Source: Foxnews Health, Press releases

Overview of approved cellular and gene therapy products by the FDA in the US and EMA in Europe

Food and Drug Administration (FDA)

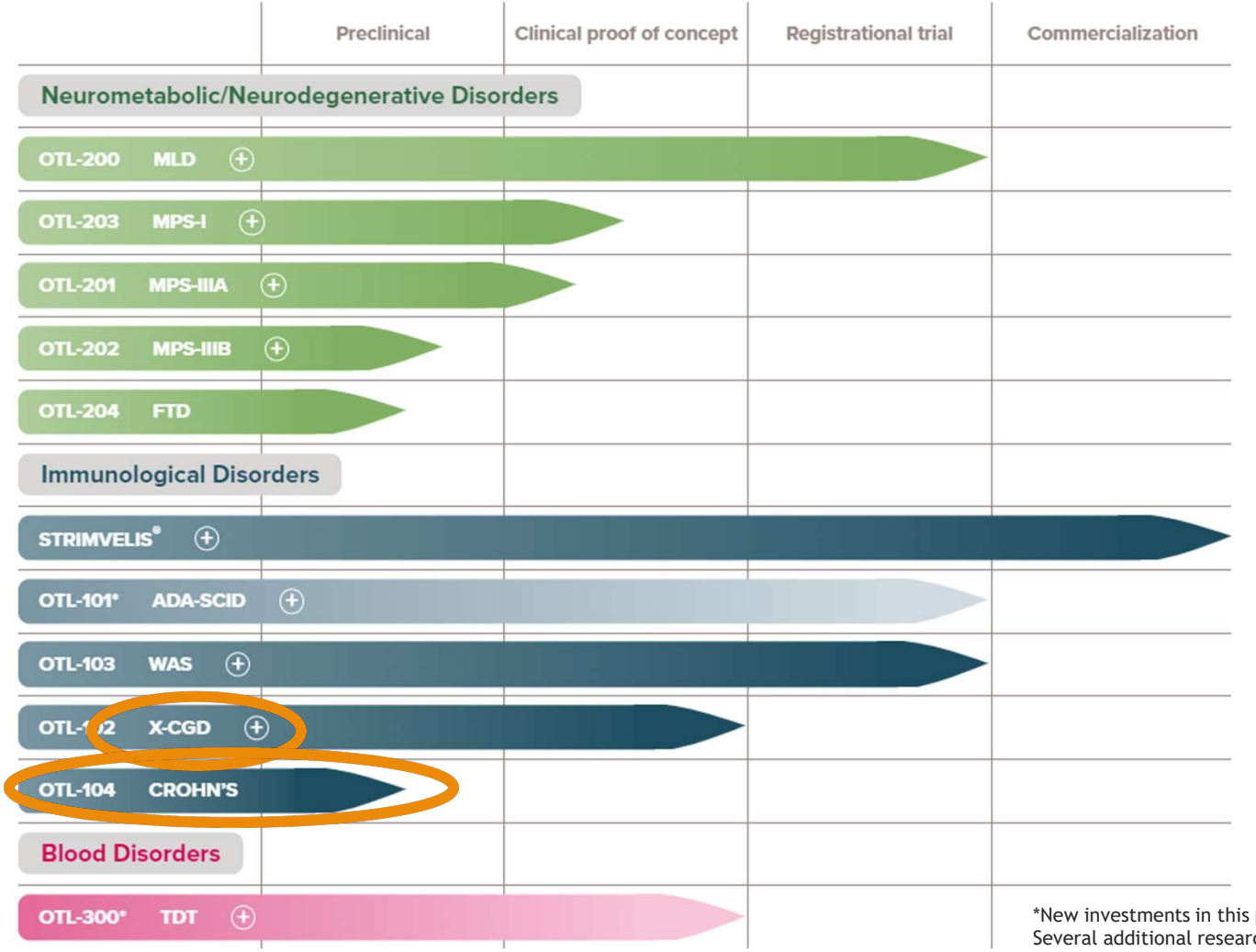
Product	Company	Indication
ALLOCORD	SSM Cardinal Glennon Medical	Therapies for **hematopoietic system** that are inherited, acquired, or result from myeloablative treatment
CLEVECORD	Cleveland Cord Blood Center	
Ducord	Duke University	
HEMACORD	New York Blood	
GINTUIT	Organogenesis	**Mucogingival** conditions
IMLYGIC	BioVex.	**Melanoma**
KYMRIAH	Novartis	B-cell acute **lymphoblastic leukemia**
LAVIV	Fibrocall Technologies	Nasolabial fold wrinkles
LUXTURNA	Spark Therapeutics	**Retinal dystrophy** caused by biallelic RPE65 mutation
MACI	Vericel	Cartilage defects
PROVENGE	Dendreon	**Prostate cancer**
TECARTUS	Kite Pharma	Mantle cell **lymphoma**
YESCARTA	Kite Pharma	Large B-cell **lymphoma**
ZOLGENSMA	AveXis	Spinal **muscular atrophy**

Source: FDA, EMA

European Medicines Agency (EMA)

Product	Company	Indication
GLYBERA	UniQure biopharma	**Hyperlipoproteinemia** Type I
IMLYGIC	Amgen	**Melanoma**
KYMRIAH	Novartis	Precursor B-Cell Lymphoblastic **Leukemia-Lymphoma**,
LUXTURNA	Spark Therapeutics Ire	**Retinal dystrophy**
STRIMVELIS	(GSK) Orchard	Severe Combined **Immunodeficiency**
YESCARTA	Kite Pharma	**Lymphoma**, Follicular **Lymphoma**, Large B-Cell, Diffuse
ZOLGENSMA	AveXis	Spinal **Muscular Atrophy**
ZYNTEGLO	bluebird bio	**beta-Thalassemia**

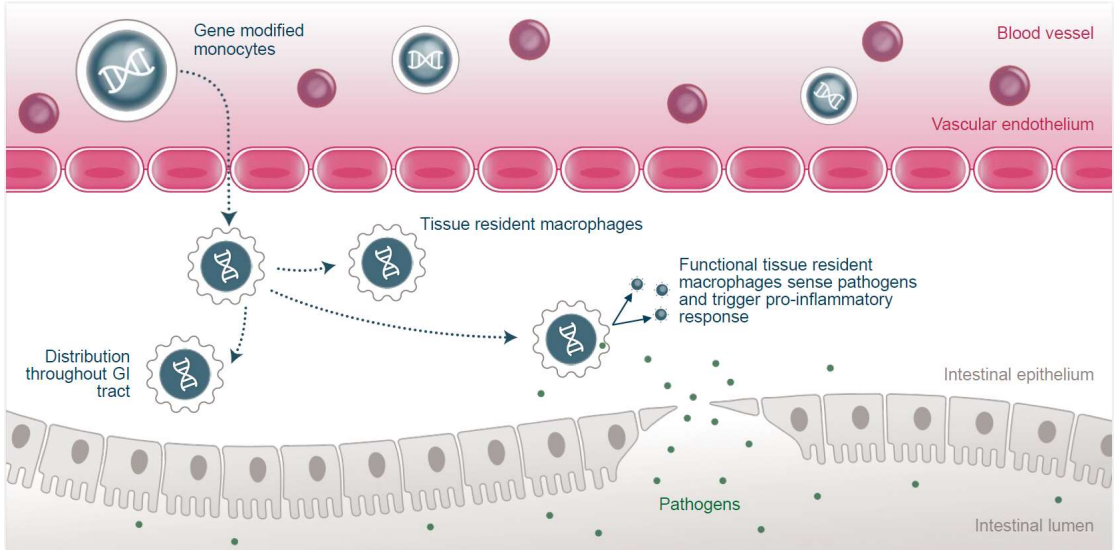
Orchard has several drugs in registrational trial that could potentially be commercialized in the future

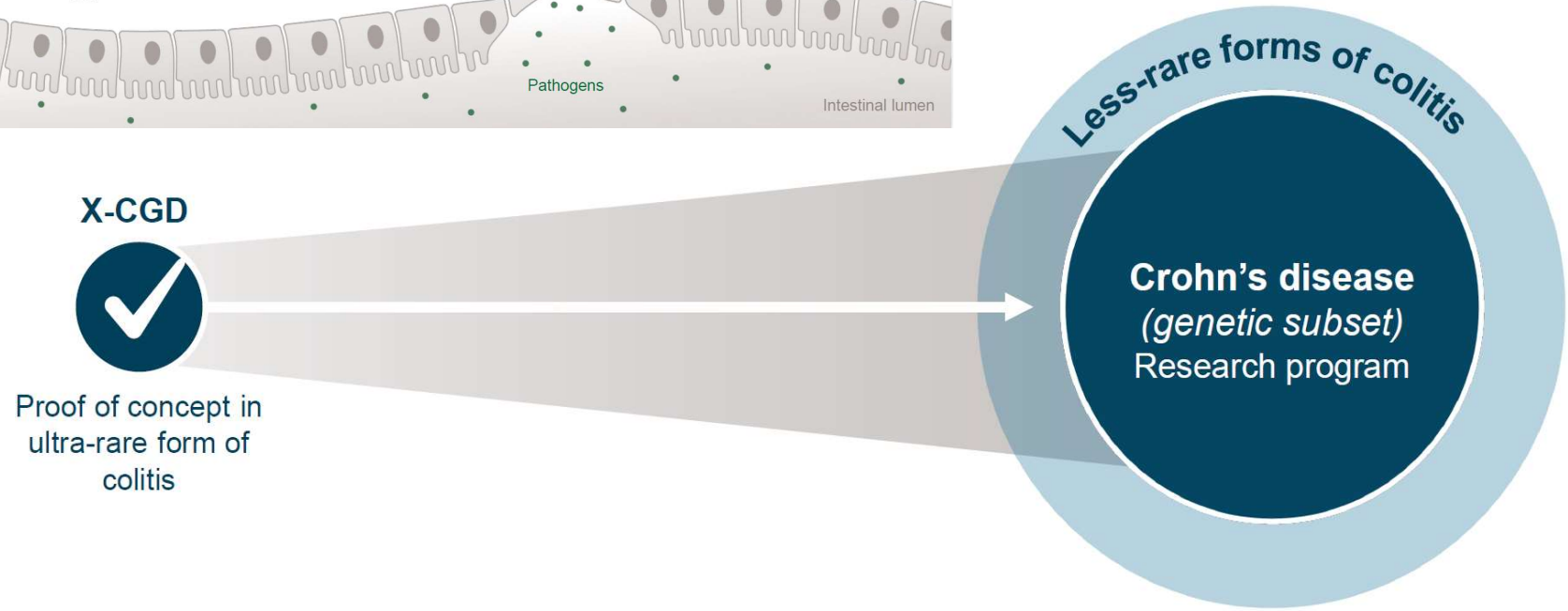


*New investments in this program are currently limited.
Several additional research and preclinical programs under development.
The investigational therapies in our pipeline have not been approved by any regulatory agency or health authority.

Source: Orchard Therapeutics website, Pipeline

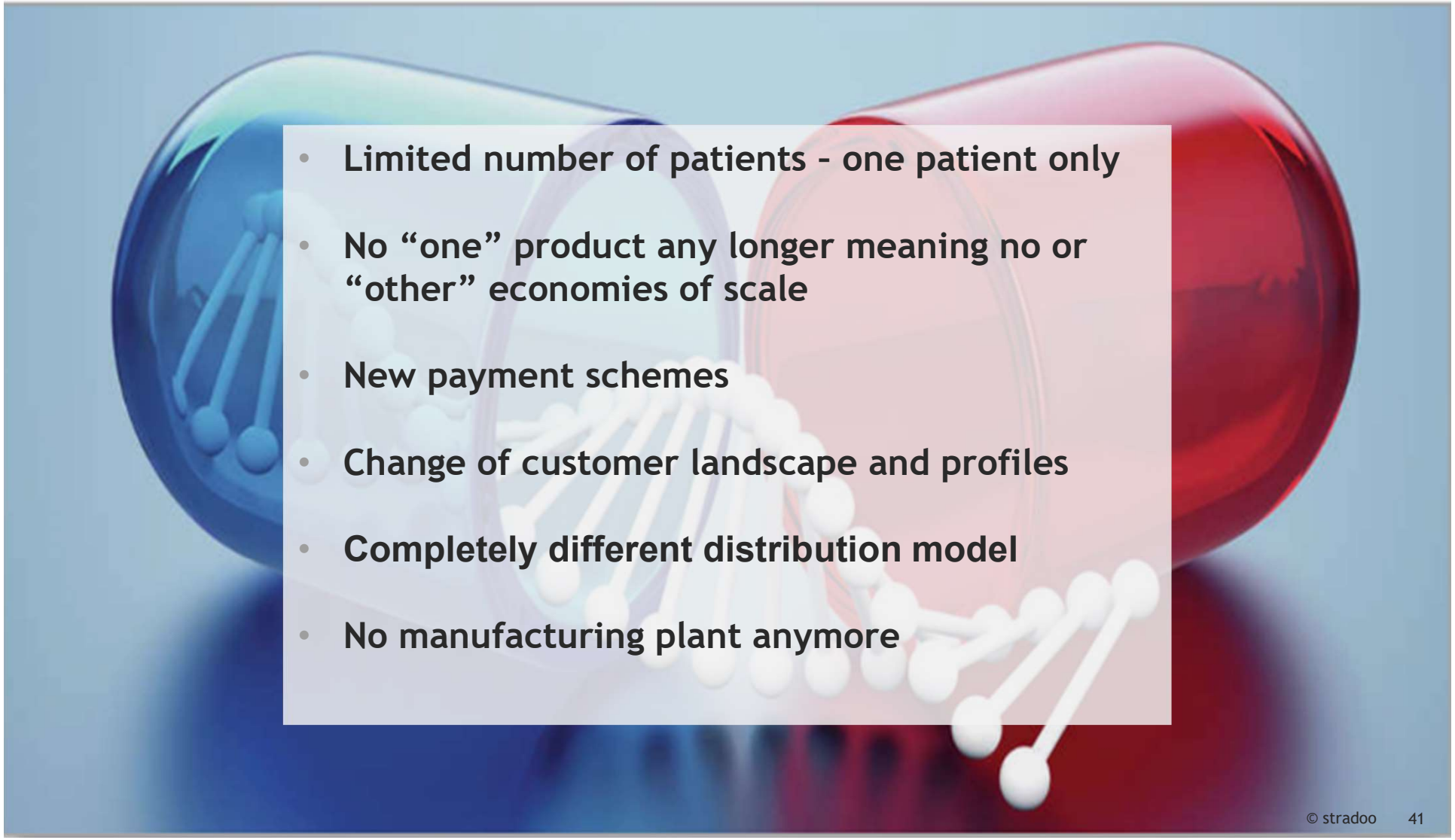
Clinical validation in X-CGD supports application in less rare populations such as Crohn's Disease





Source: Orchard Therapeutics Corporate Presentation, Aug 2020

Personalized Medicine does not have much of the old Pharma model any longer – new business models are to be developed



- Limited number of patients – one patient only
- No “one” product any longer meaning no or “other” economies of scale
- New payment schemes
- Change of customer landscape and profiles
- Completely different distribution model
- No manufacturing plant anymore

Digital therapeutics have become an integral part of diagnose and treatment

Plenty of companies are working especially on DTx for chronic diseases often establishing commercial partnerships with Pharma

- There is currently a **larger number of facilities working on multiple DTx** to treat different types of indications, from chronic illnesses to addiction medicine to mental health and rehabilitation and beyond
- **Most applications are in the area of chronic diseases** (with the exception of mental health problems) and offer disease-treating relevant approaches; DTxs that actually need to be prescribed, as well as DTxs that are set up for self-consumption with less clinical approach
- **In 2019 multiple "digital health-partnerships" between pharma and tech-companies that aim at digital health solutions could be witnessed**, including big players from both industries like Bayer, Johnson-Johnson, Pfizer, Novartis, Merck, GSK, Sanofi, Apple, Google and many more

Source: stradoo

An increasing number of approved DTx complements the various PSPs that are already available on the market

	App	Indication	Configuration	Price	Regulatory
	My Pain diary and Symptoms	Chronic pain diseases and anxiety	**PSP** - Pain tracking, monitoring and management	5.49 €; 1000 – 5000 DNLDs	No approval or prescription necessary
MMP	**Manage my Pain**	Arthritis & rheumatism, cancer, chronic pain, migraines, Fibromyalgia	**PSP** - Pain tracking, monitoring and management	Free(Lite), 3.99 € (Pro); 50 - 100.000 Downloads	No approval or prescription necessary
Sleepio	**Sleepio**	Sleep improvement	**PSP** – Teaching of user based cognitive behavioral therapy (CBT)	Weekly subscription fee of 17.99 €	No approval or prescription necessary
	Endeavor Rx	Treatment of children with ADHD	**DTx** – Gameplay designed to challenge a child's brain during treatment, requiring attention and focus on multiple tasks	No price information, **Prescription necessary**	**Received FDA approval in 2020**
	Natural cycles	Birth control	**DTx** – AI software that tracks fertility on the basis of data from past menstrual cycles and body temperature	Monthly subscription fee of 5.40 €	**Received FDA approval in 2018**
vorvida®	**vorvida**	Alcohol abuse	**DTx** - AI software to treat alcohol misuse identifying triggers and reducing drinking patterns	No price information, **Prescription necessary**	**Under FDA approval investigation**

Source: stradoo

All stakeholders involved in treatment/therapies will profit from a DTx

Stakeholder	Value proposition	Desired outcome
Patients	• **Help patients** suffering from a specific indication in their journey by delivering a multidisciplinary treatment solution: ○ **Patient education** ○ **Approved non-drug treatment** ○ **Adherence** ○ **Safety, monitoring & physician communication**	**Manage own disease & better communicate to physician**
Payors	• **Help payers** manage the cost burden of treatment/therapy through a cost effective multimodal solution: ○ **Improved cost effectiveness** and **patient outcomes** ○ **Performance based contracts** ○ **Real time analytics**	**Disease management via adherence monitoring**
Physicians	• **Help HCPs** provide an individualized, tailored and integrated care solution to patients suffering from a specific indication: ○ **Improved** patient outcomes, patient care, treatment options/tailored decisions and data ○ **Less** face **consultations** and **faster consultation** times ○ **Treatment** option with **low risk profile**	**Obtaining most relevant information on health status**

Source: stradoo

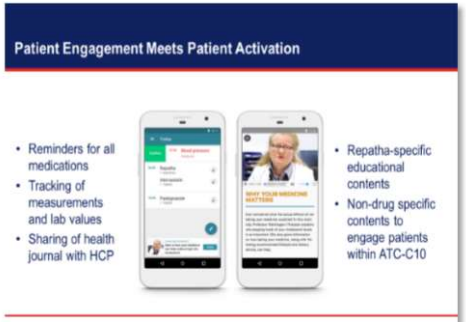
Based on great experience, Smartpatient.eu has provided significant insights during market interviews – further dialogue recommended

MyTherapy by Smartpatient.eu

smart patient

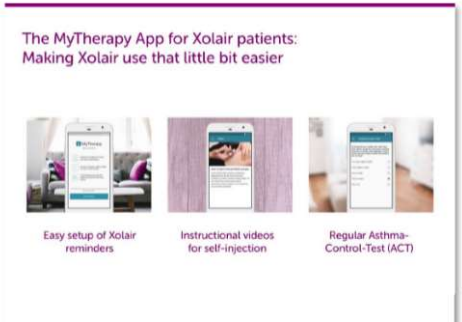
- >4 million users (fastest growing worldwide)
- 89% patient adherence
- 76% 30-day retention, 53% used the App >12 months
- Avg. 4.8 stars in 70000 App store reviews
- Best rated disease management platform

AMGEN



Stand-alone app module for patient engagement and activation

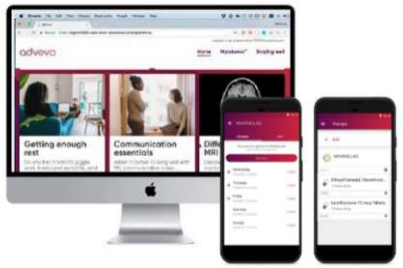
- Patient engagement with in-app reminders and 'Repatha'-specific content in the context of injection
- Patient activation via product-agnostic educational contents for users on lipid lowering therapy



Supporting safety and persistence for launch of Xolair home use

- Lean offering supporting home use approval
- Custom, label compliant setup of reminders + injection videos + ePROs
- Roll-out to >10 markets in year 1

MERCK



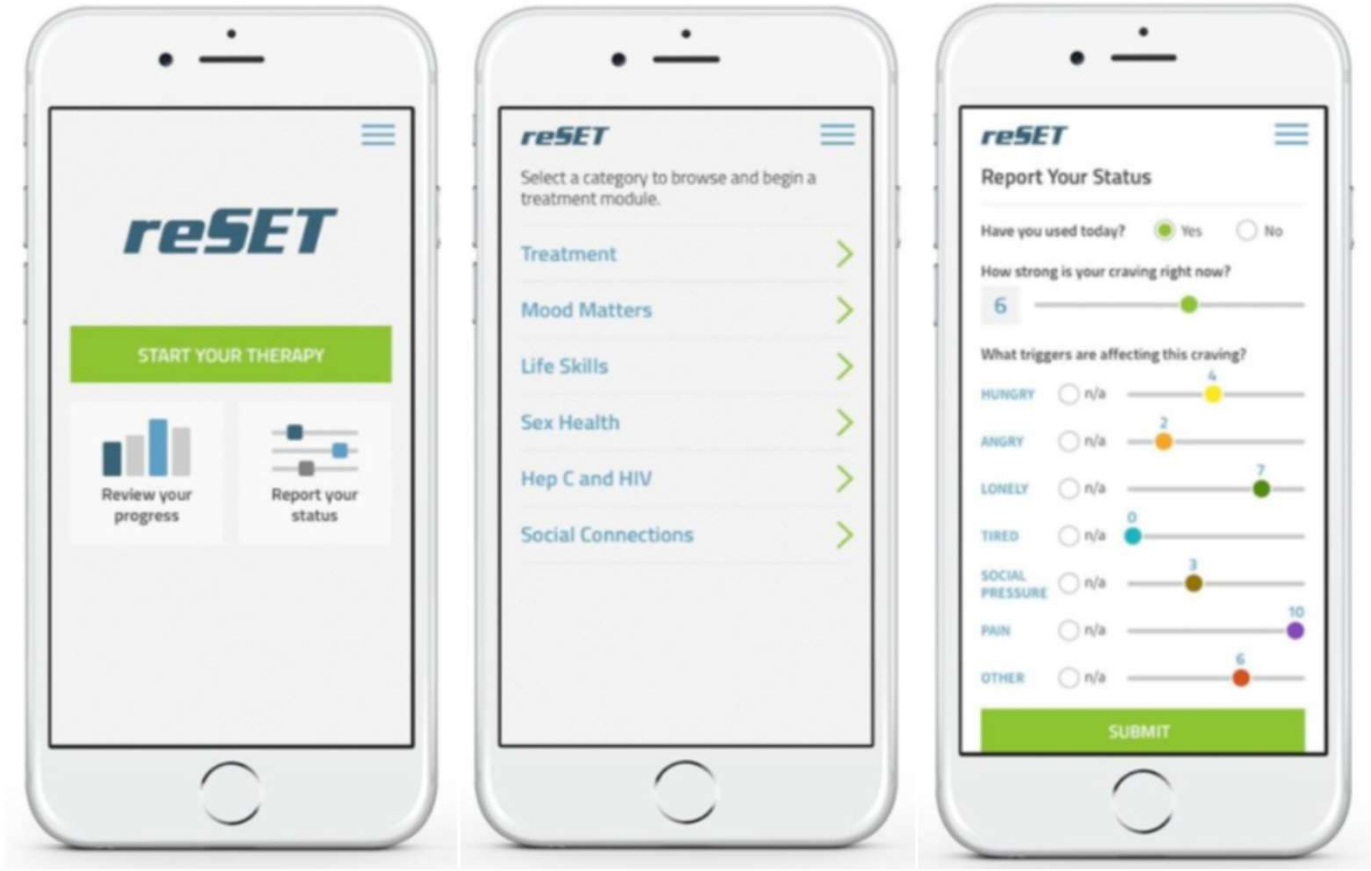
Global multichannel patient support program ('adveva')

- Implementing a persistence-oriented care pathway across web, app and phone, incl. data sharing via CRM
- Global roll-out to 20+ markets with wildly different requirements

NOVARTIS

Source: smartpatient.eu

reSET and reSET-O serves an therapeutic addition to outpatient treatment for patients with a “substance use disorder”



- **reSET** is a 90-day prescription digital therapeutic for **substance use disorder** and illustrates a **cognitive behavioral therapy**
- **reSET-O** is an 84-day prescription digital therapeutic for **opioid use disorder** designed to **increase retention** of patients out of hospital
- Both platforms feature associated **dashboards for HCPs** to view information about the patients’ use etc.

Source: reset, reset-O

Beats Medical provides individual, daily exercises for the Mobility, Speech and Dexterity symptoms of Parkinson patients

Mobility

- The application provides **individually tailored metronome therapy** via iPhone
- Metronome therapy provides an auditory cue to address the mobility symptoms of Parkinson‘s each day

Speech

- The application provides **daily speech and language therapy exercises** with real-time visual feedback aimed at speaking loudly and clearly
- The speech and language therapy works on **vocal volume, intonation and voice clarity**

Dexterity

- Based on recognized dexterity exercises for Parkinson, the application provides **daily occupational hand therapy exercises**
- This helps with fine hand movement issues such as difficulties with doing up buttons, zippers or handwriting

Source: Beats Medical

Beats Medical Dyspraxia App is designed to complement therapy plans in order to address the needs of children living with Dyspraxia

01| App Menu

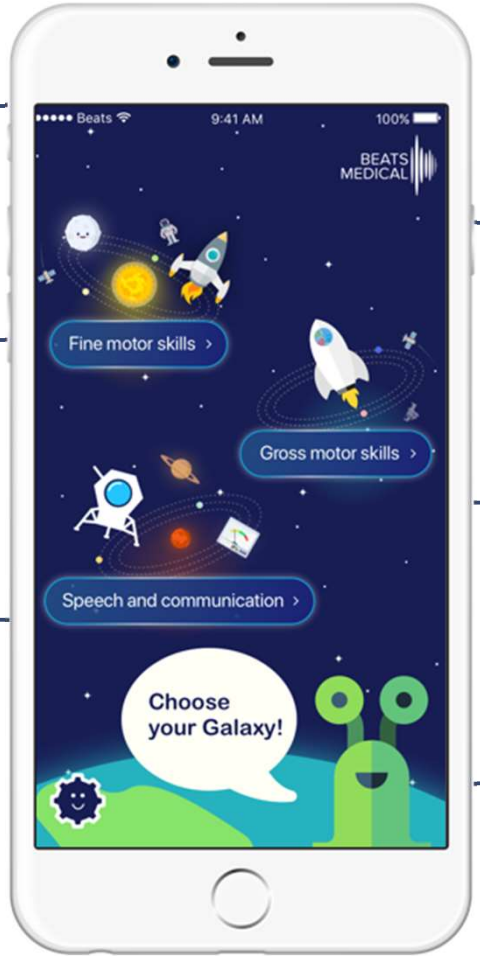
Easy-to-use, child friendly interface

03| Space Race Game

Fun space theme designed to help engage the child

05| Gross Motor Game

Instructions onscreen to encourage the child to take part in physical exercises



02| Fine Motor Menu

Choice of games to help with fine motor skills

04| Gross Motor Menu

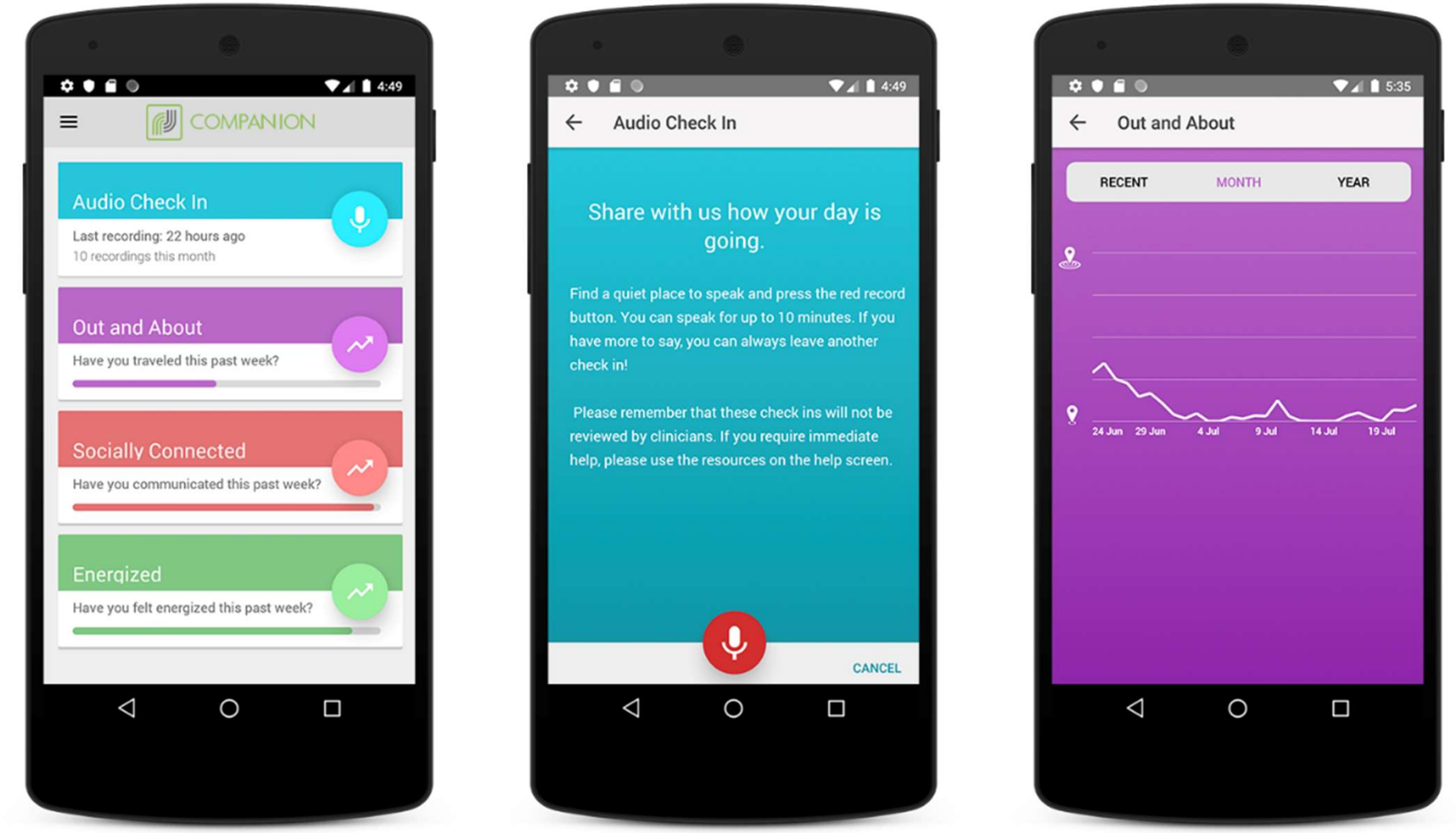
A variety of exercises to help with gross motor skills

06| Speech Game

Daily exercises to promote communication, with an emphasis on clarity and diction

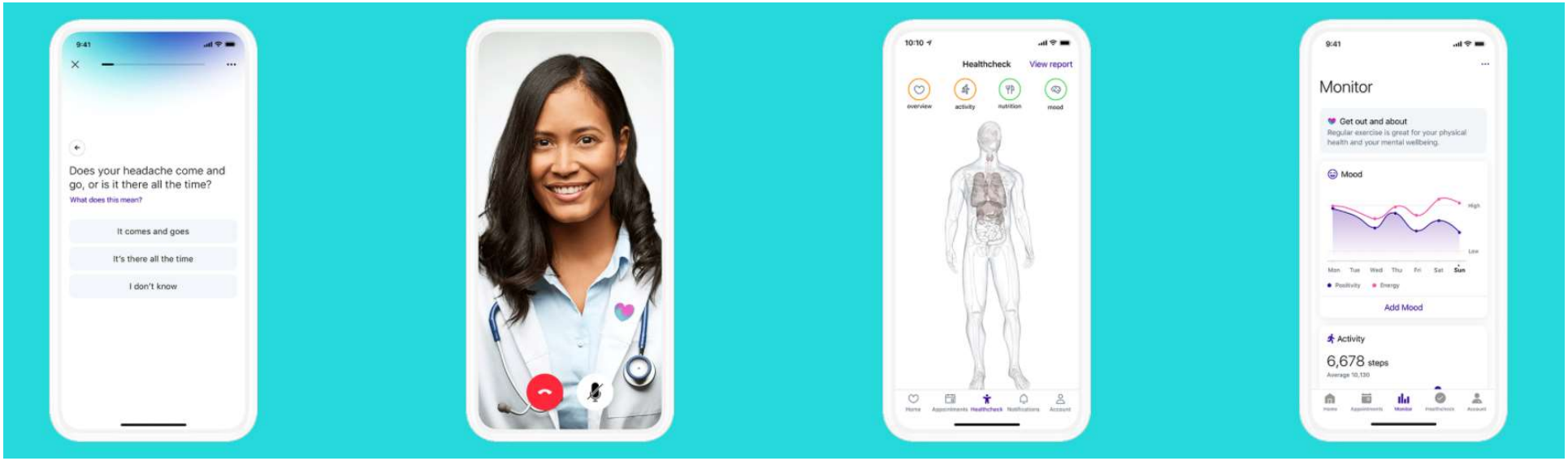
Source: Beats Medical

The CompanionMX® system uses AI-enabled voice analysis to allow clinicians to track patients‘ mental health



Source: CcompanionMX

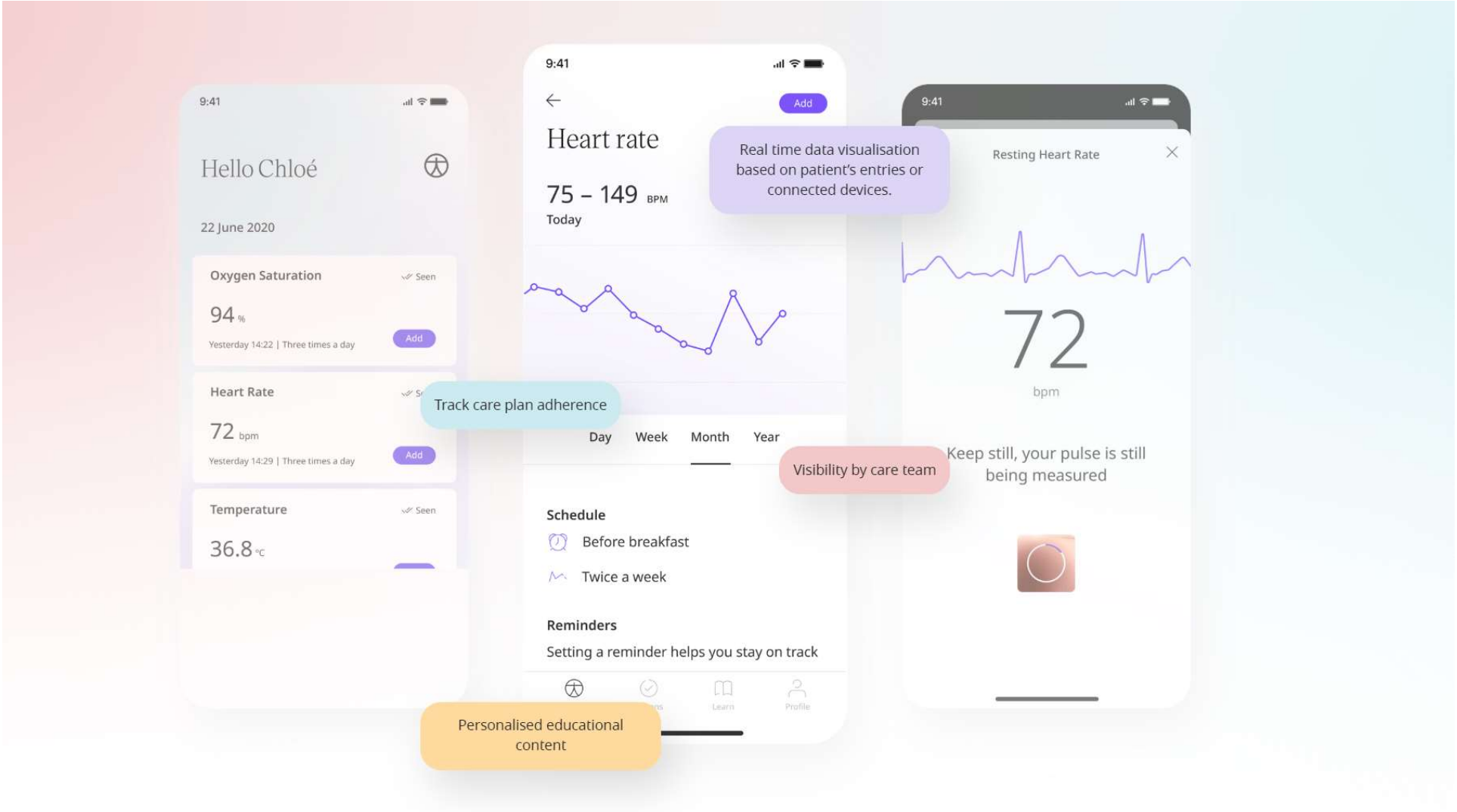
Babylon Health is a app …market cap 2 $bn



- **People can "Ask Babylon"** to **inquire** about **medical concerns** to get an initial understanding of what they might be dealing with
- Babylon offers a **"talk to a doctor"** service via its app; **"GP at Hand"** that provides **24/7 access to healthcare professionals** through video or audio conferencing
- At the consultation**, doctors can give medical advice**, answer questions, discuss treatment, and can order prescriptions that can **be delivered to the patient**

Source: Babylon website

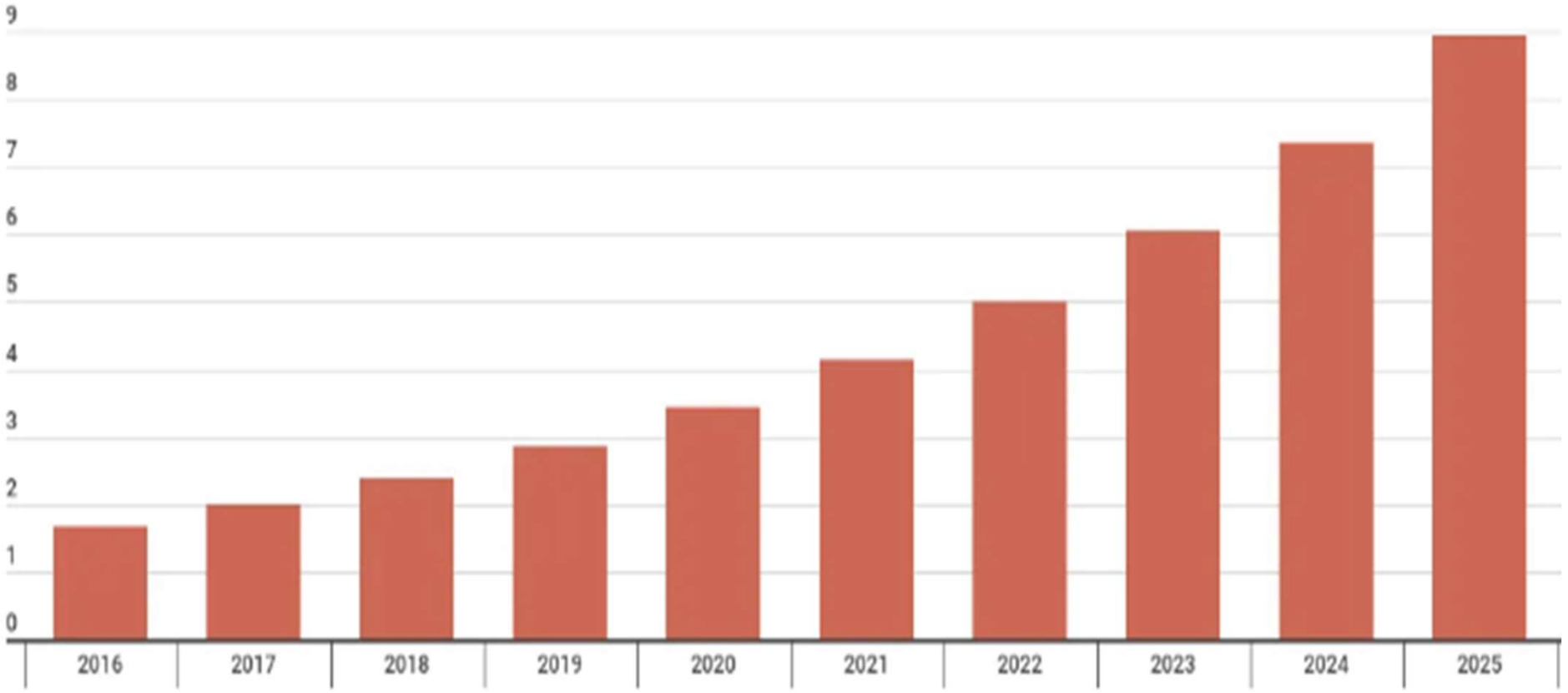
Medopad/Huma® has specialized in remote patient monitoring for patients focused in finding „digital biomarkers



Source: Huma website

The digital therapeutics market is forecasted to grow significantly in the coming years

Global DTx revenues forecast ($bn)

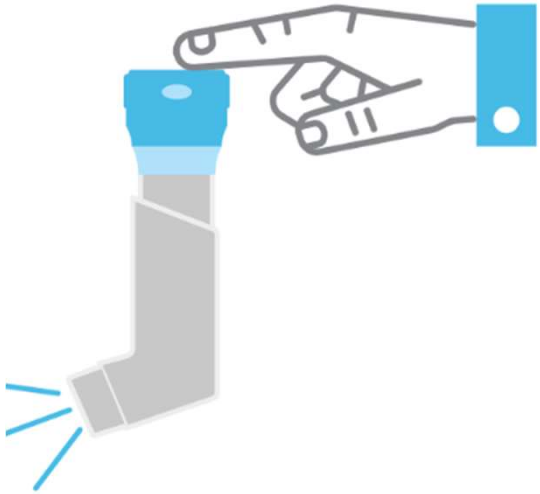


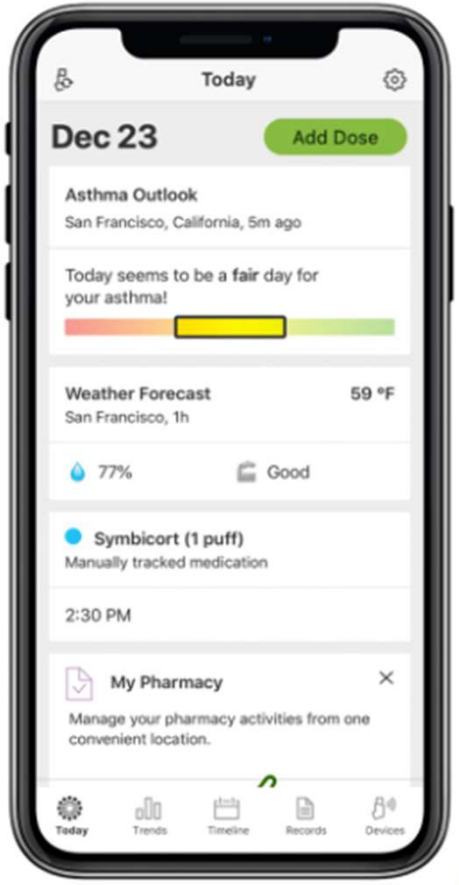
Source: Insight Partners 2018 via Statistica

ProAir® digihaler measures the inspiratory flow of patients, automatically generates data and sends it to the respective HCPs

Source: ProAir

Propeller's Breezhaler® is a smart device that increases the number of symptom-free days by simplifying the management of Asthma and COPD





- The Propeller sensor can simply be attached to the inhaler
- The device **collects and records data each time the pump is being used** and enables HCPs as well as family members to manage use via the mobile app

Source: Propeller

Ancon® Medical provides nanoparticle biomarker tagging (NBT) for disease detection

- Diseases produce a **specific mixture of molecules**, which act as so-called **"biomarkers"** that indicate the **presence of a disease**
- **Biomarker Tagging (NBT) detects deadly diseases**

- NBT offers a very **high sensitivity** for **biomarker detection** as it can detect their presence with concentrations of a **billion times less than other air molecules** (nitrogen, oxygen, carbon dioxide and other abundant molecules)
- NBT can detect **butylated hydroxytoluene**, the **lung cancer biomarker** molecule, in exhaled breath in **only a few minutes.**
- The **reliability** of **breath detection** for lung cancer was proven in tests against **chest CT scans**

Source: Ancon Medical

The smart catheter “UroSense” is a medical device that uses smart software to analyse urine for diseases like diabetes

- Catheter fitted with a transmitter that can **monitor urine output and core body temperature** for patients on catheterization
- In combination with the software, **reports are automatically generated** and **sent to HCPs** in order to enhance disease management and monitoring

- Smart monitoring **helps to spot** the signs of
  - **Infection**
  - **Cancer**
  - **Diabetes**
  - **…**

…therefore creating better treatment plans and prevention options

Source: UroSense

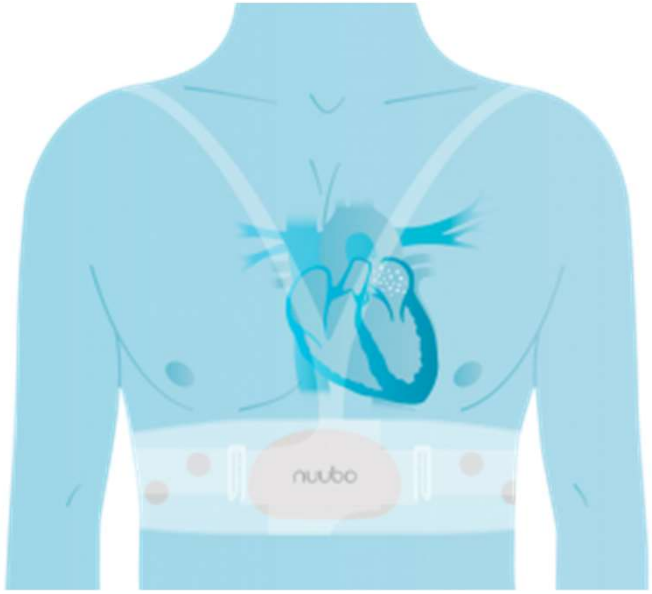
The CardioQore illustrates a smart ECG-device for the everyday monitoring of patients with cardiac diseases

- **Continuous ECG** monitor designed to **provide medical grade data**
- Device can be **worn within the normal lifestyle of users**: at work, at the gym etc.
- **Data** are automatically **recorded via the mobile app**
- Information can be **sent to HCPs for analysis** without the need for physical visits

Source: CardioQore

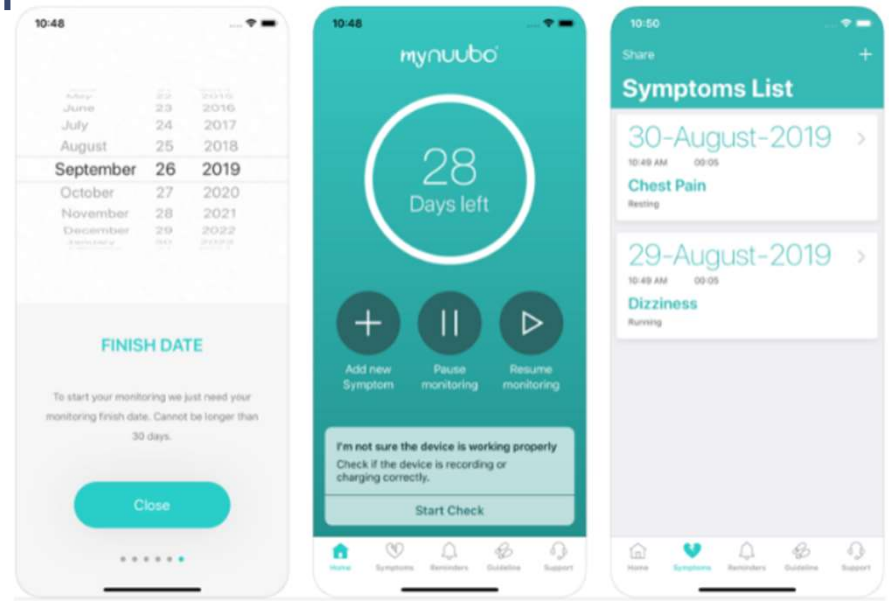
Nuubo® is a wearable ambulatory ECG monitor, which continuously records and analyses every single heart-beat

The smart-vest



- The vest comes with **AECG technology** and is **wearable for up to 30 days**
- It is **wireless** and very easy to hook up
- It allows to detect cardiac abnormalities that are asymptomatic (no symptoms)

The mobile application

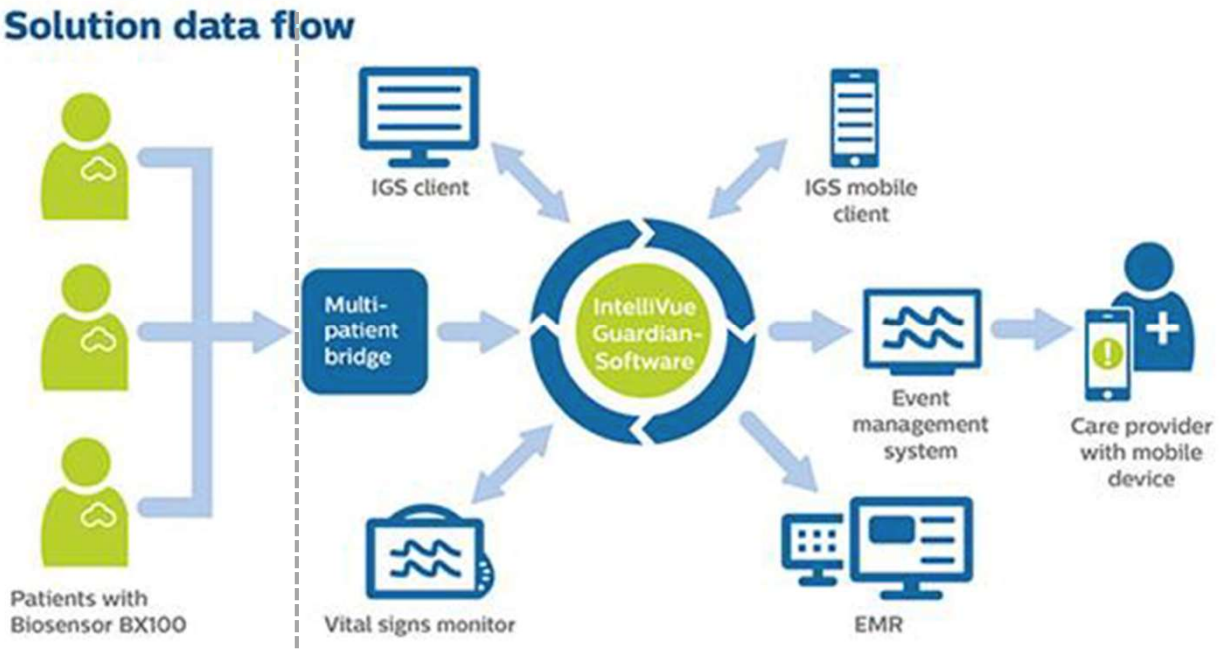


- The mobile app **shows patients how to use the vest** during their monitoring time, but **does not interact with the device**
- It allows to **record symptoms whenever needed** and to **directly share them** with the respective HCP

Source: Nuubo

Phillips' Biosensor allows clinicians to record vital data of patients who require constant monitoring in a hospital setting

- Device designed to **keep watch of patients** in need of frequent monitoring

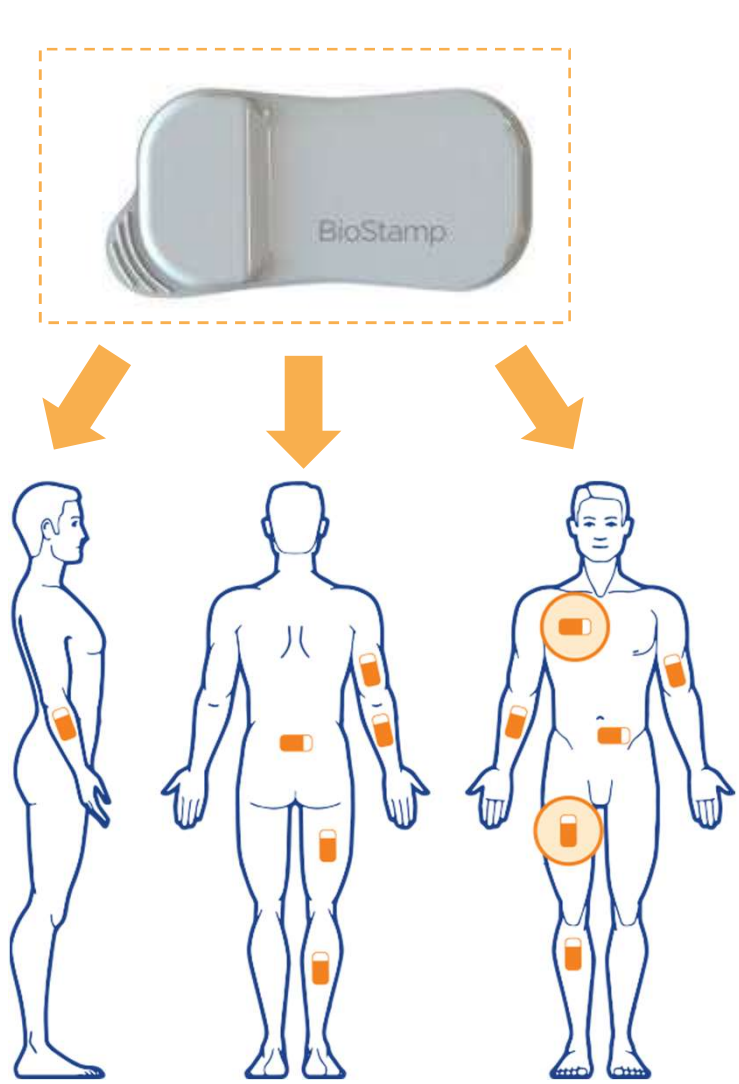


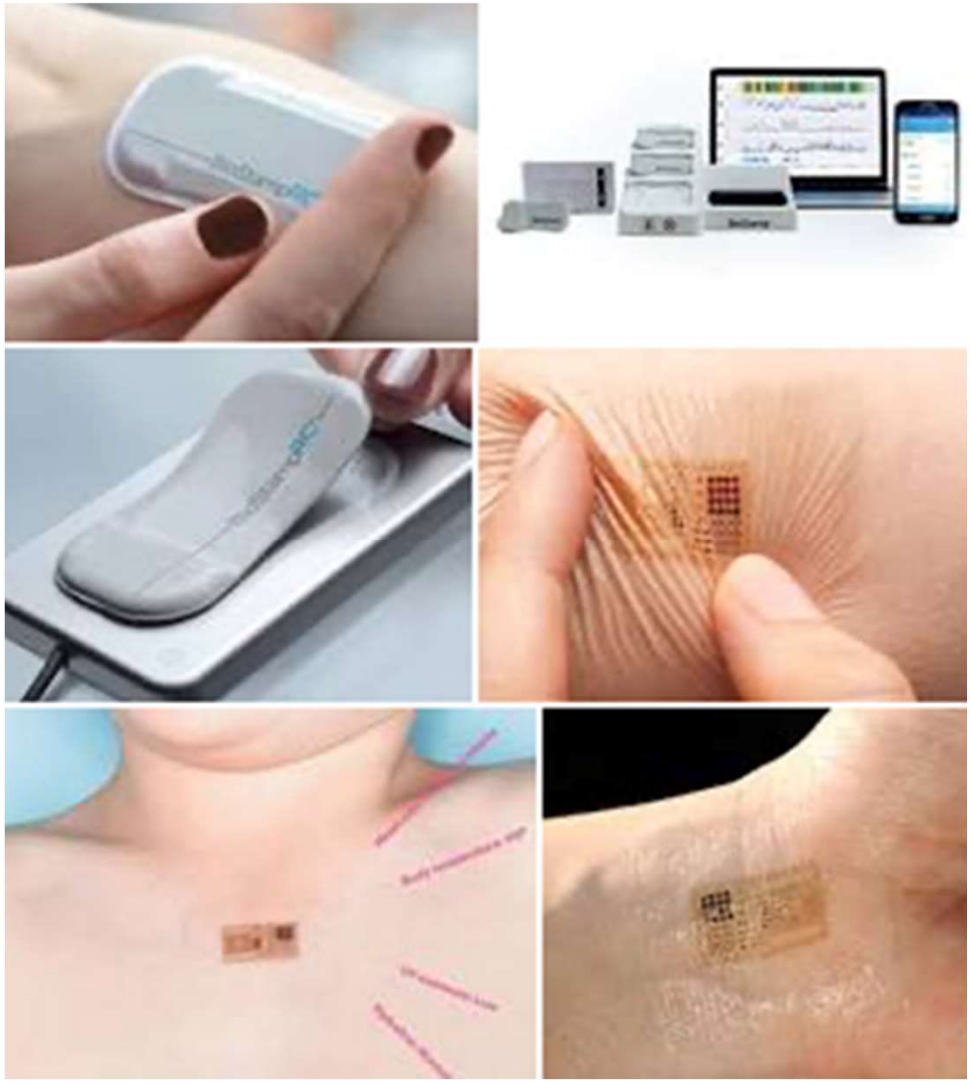
- Sensor simultaneously **gathers patient vital signs and critical data**, including **heart rate**, **respiratory rate**, **skin temperature**, **body posture**, **fall detection**, **single-lead ECG**, **R-R interval** (RR-I) and **step count**

- **Transmission of vital data to clinical information systems** in order to enhance clinical workflow

Source: Phllips

The BioStamp® nPoint is a cleared medical device designed to collect medical grade data in clinical trial setting





Source: BioStamp

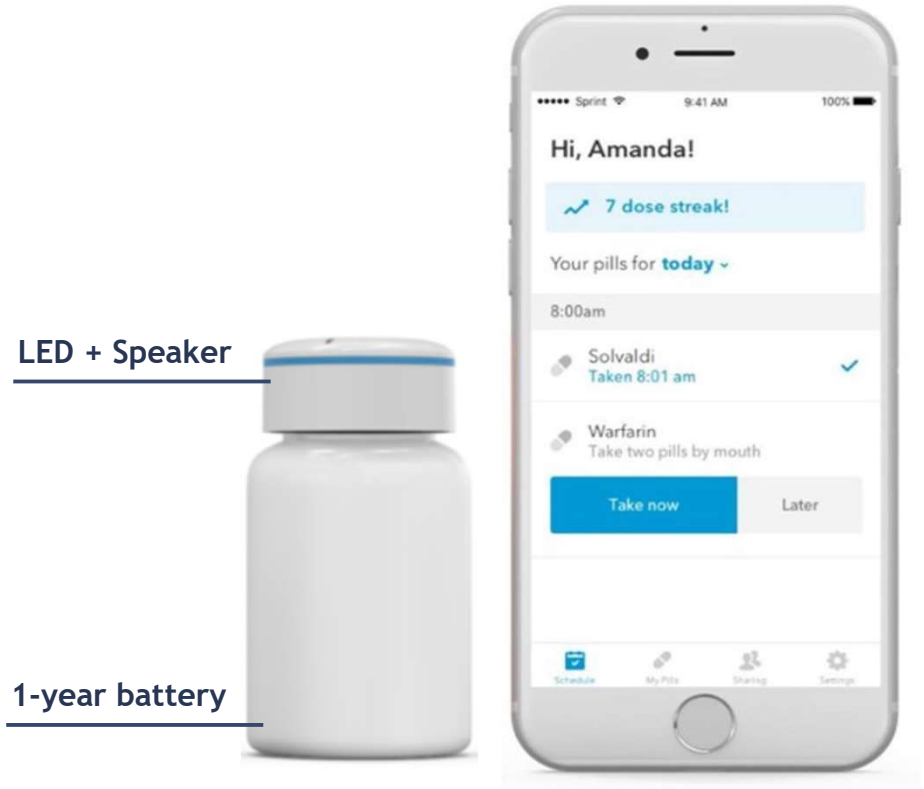
Accelerated by innovative solutions, adherence has become an integral aspect of treatment

Deliverables of adherence solutions

- Adherence is directly correlating with **clinically relevant parameters** and treatment **outcome**
- **Technological ecosystems** of automated devices and monitoring aids produce **transparency** on patient adherence
- Data **collected in electronic monitoring and tracking systems** stimulate patients to remain adherent and allow physicians/caregivers to monitor
- **Increase of therapy outcome** by **transparent feedback on adherence**

Source: Proteus / Xhale / eTect / stradoo research

Pillsy® allows patients to keep track of their medications and automatically orders new medication at demand



Automatic tracking

- The device **automatically tracks when the bottle is opened** and will mark the dose as "taken" if you have a scheduled dose

Intelligent reminders

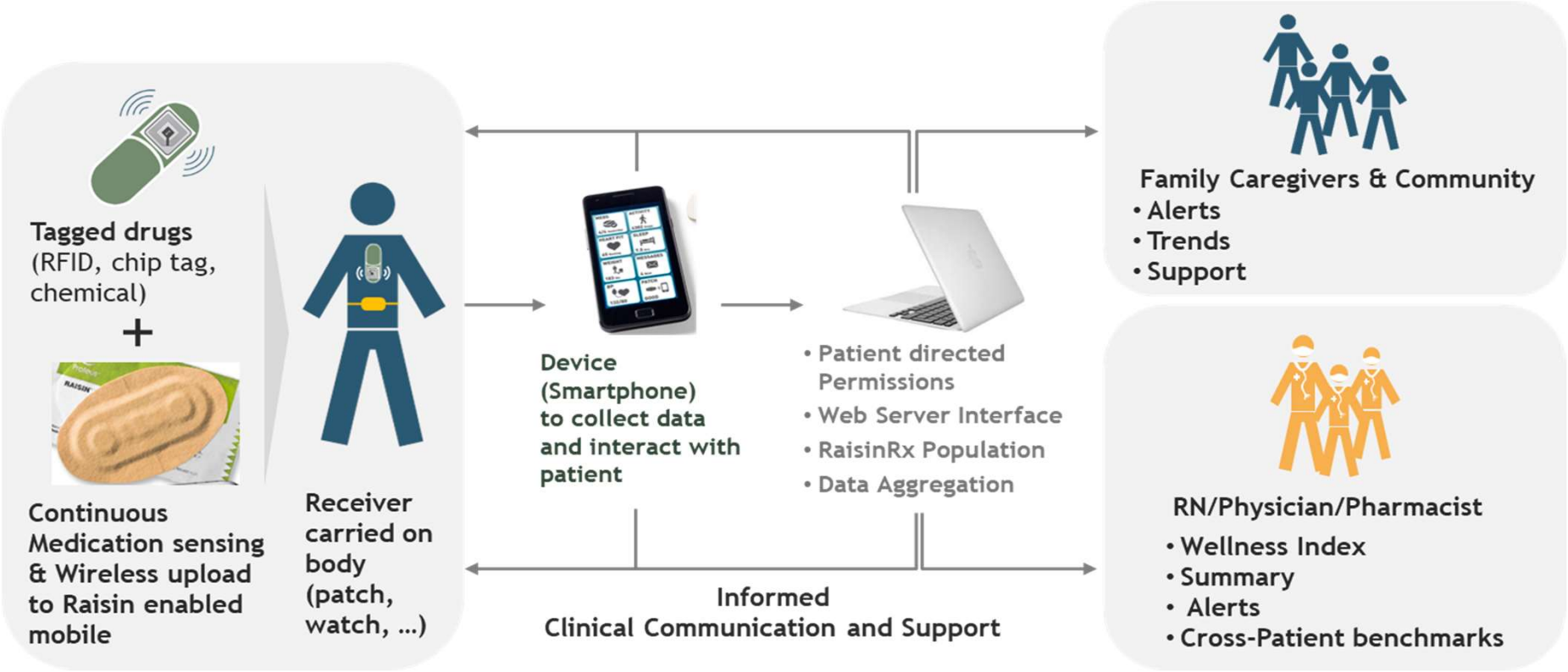
- Pillsy® **beeps and blinks if the dose has not been opened** during the scheduled dose period and **sends notifications** on the patient's phone

View history

- The **pill history can be examined** at any time in app's drop-down calendar

Source: Pillsy

Proteus® has collected more than $ 500 mill. in funding – collaborations with Otsuka, Novartis and many other Big Pharma

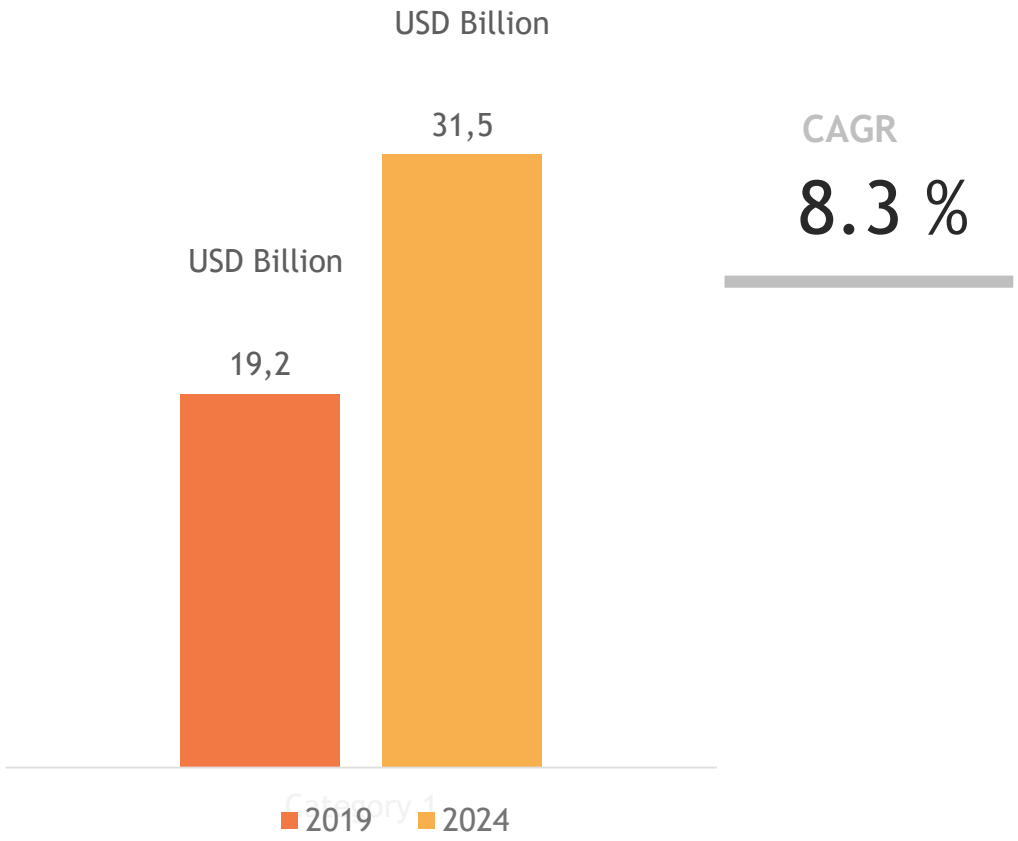


- **3 key components: ingestible sensor** the size of a grain of sand; wearable **sensor patch**; **mobile app** and **provider portal**
- Activated as soon as the medication is taken: Once the ingestible sensor reaches the stomach, **it transmits a signal to a patch**
- A **digital record is automatically generated** and sent to the patient's mobile device and the Proteus cloud from where it **can be accessed by the HCP**

Source: Proteus

The global Biosensor market size is expected to grow from USD 19.2 billion in 2019 and reach USD 31.5 billion by 2024

Outlook on opportunities in Biosensor market 2019-2024



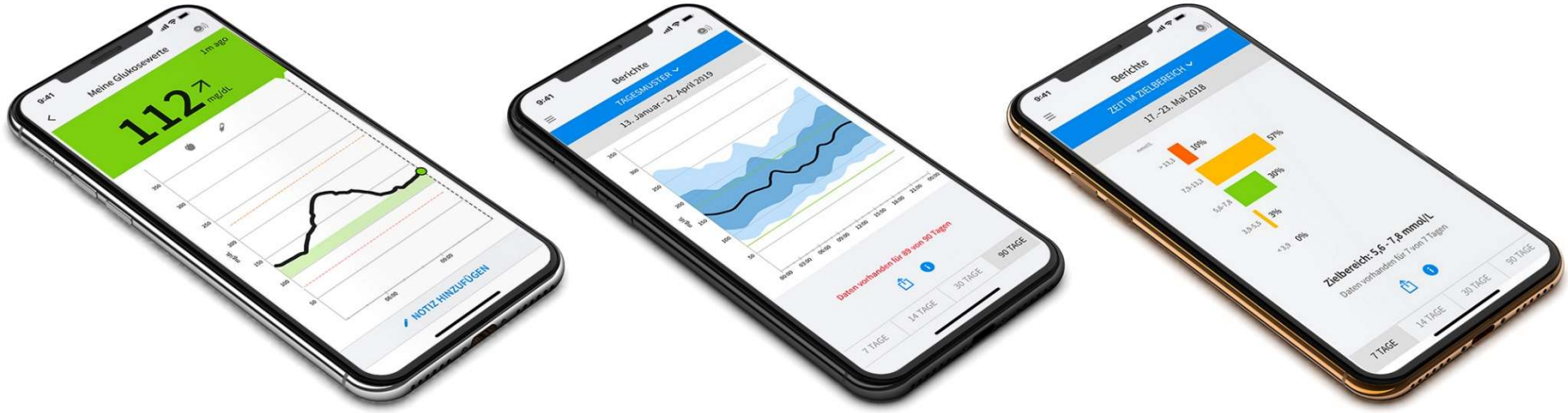
CAGR

8.3 %

Source: Market research report

FreeStyle Libre® enables continuous glucose monitoring and eliminates the need for finger sticks

- **Wearable sensor** the size of two stacked quarters is placed on the back of the upper arm
- The wearer **uses a smartphone to get real-time glucose measurements** by holding it close to the sensor
- Mobile app displays **current glucose levels**, information on whether **glucose levels are rising or falling**, and **trends in glucose levels** over periods up to three months



Source: FreeStyle Libre

The Dexcom® G6 CGM system is a continuous glucose monitoring device that translates glucose measurements into dynamic data to illustrate direction of change

Control glucose level

- Dexcom CGM is proven to lower A1C, reduce hypoglycemic incidents, and helps to determine a trend in glucose levels

No finger sticks

- The Dexcom G6 is permitted by the FDA to make diabetes treatment decisions without confirmatory finger sticks or calibration

Customizable Alerts & Alarms

- The current glucose level can always be read off
- It allows to set a range to get notified when the glucose level heads too high or too low

Sharing of Glucose Data

- The gathered information can be stored and shared with up to 10 followers via the application

Source: Dexcom

Bigfoot Medical® developed a whole system of glucose meters and pens in order to ease the diabetes treatment for patients

- Program that depicts an **integrated system to help patients dosing their insulin** more easily and accurately
  - The system consists of a **mobile phone app**, **proprietary insulin pen caps**, **pen needles** and **glucose sensing technology**
    - Bigfoot's platform connects these different parts **and uses algorithms to predict blood glucose levels** and **calculate recommended doses of insulin**
      - The system received an **FDA breakthrough device designation** and will require a pivotal clinical trial and subsequent regulatory approvals

Source: Bigfoot Medical

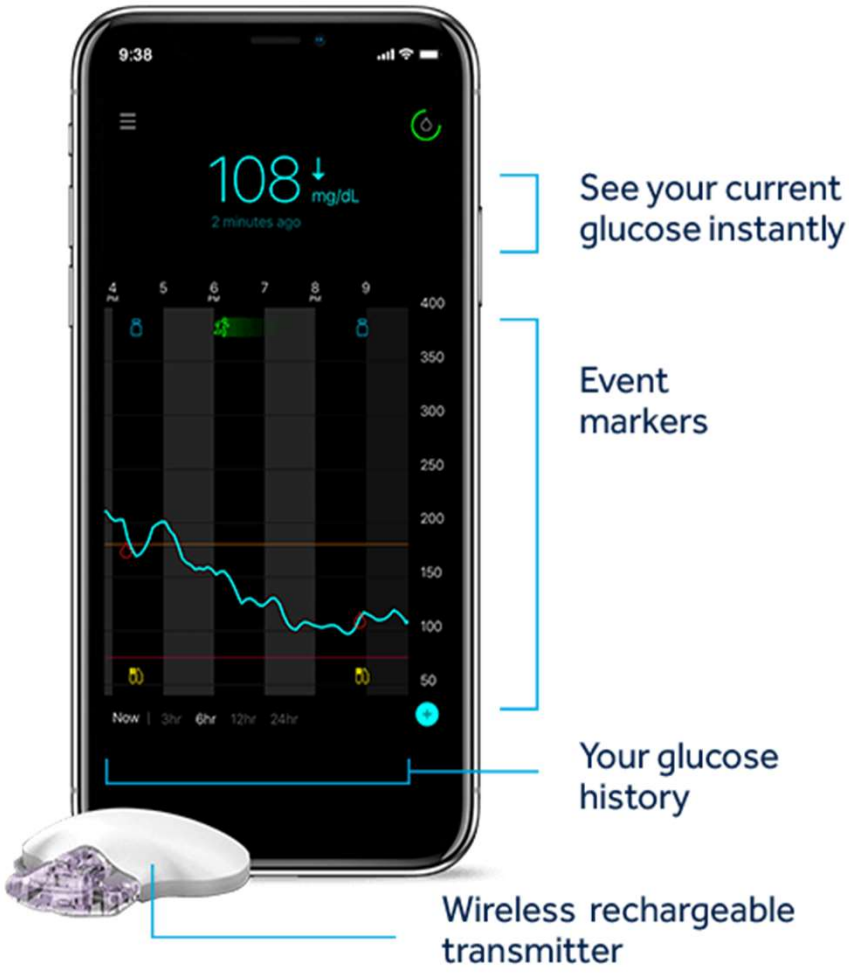
Medtronic's pump system imitates a human pancreas by automatically adjusting the insulin injections based on the current glucose levels

Medtronic

- **Portable smart pump system** that delivers insulin through a hidden tube into the patient's body
- The device allows for the **injection of very small volumes** and the ability to deliver fluids at **precisely programmed rates** or automated intervals
  - Every 5 minutes, the Auto Mode determines whether to deliver insulin and **automatically adjusts injection levels**, based on the body's needs

Source: Medtronic

The Guardian Connect® System can be integrated into Medtronic's pump system, thereby constructing an artificial pancreas



- The **wearable sensor continuously measures glucose levels** in the interstitial fluid and is connected to the transmitter
- The transmitter **sends glucose readings approx. every 5 minutes to the phone app** via Bluetooth

Medtronic

- The **mobile app** displays sensor **glucose data and trends** right on the phone at any time
- The app automatically sends out **predictive alerts of high and low glucose events** up to 60 minutes in advance

- Connects with care partners and healthcare professionals (HCPs) via a system platform to enable care partner remote monitoring and therapy optimization

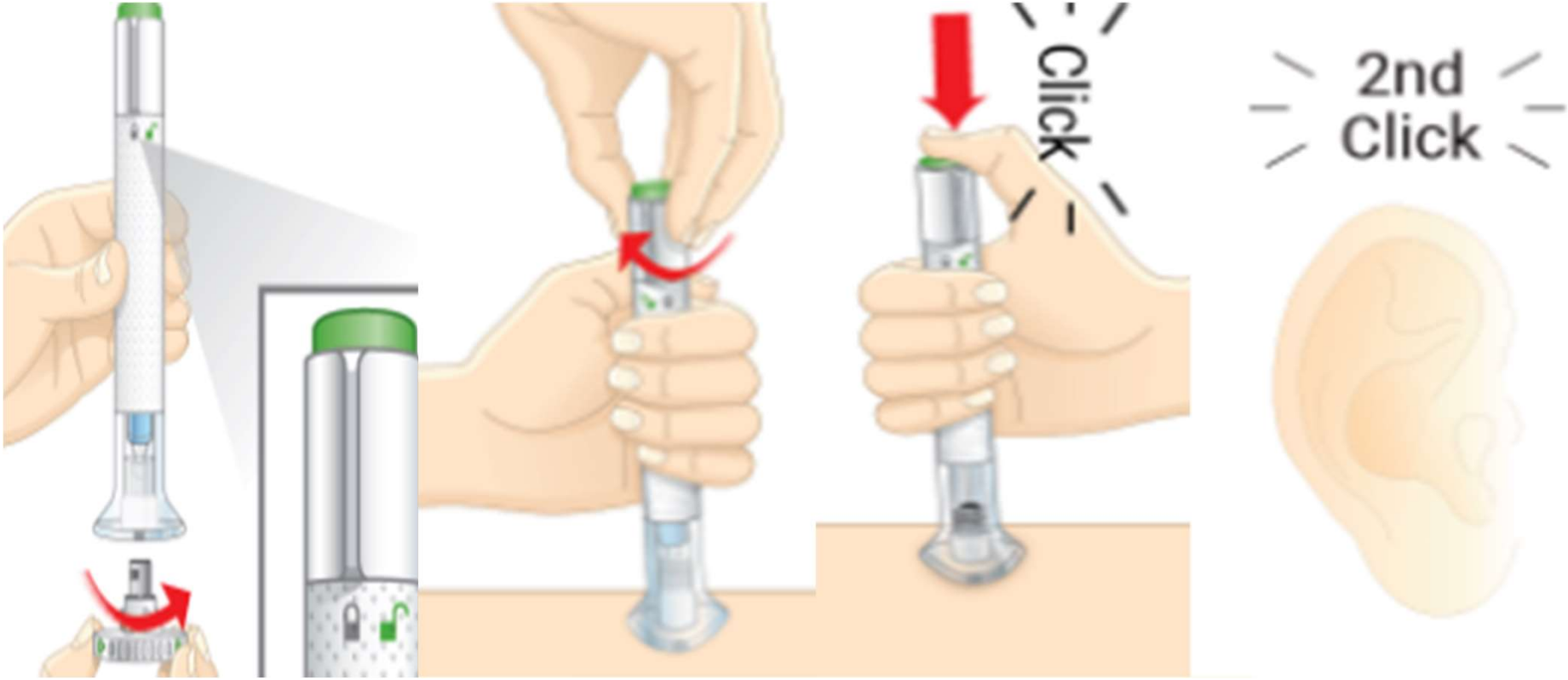
Source: Guardian

Glucowise® is a smart device which is envisioned to be the first non-invasive glucose meter on the market

- **Non-invasive glucose monitor**, which is **currently in development by META** and envisioned to be a 100% pain-free device
- A **unique sensor technology will allow Diabetes patients to monitor blood glucose levels** multiple times **without requiring skin piercing**
- AI will use the patients' current and historical data to **calculate and forecast immediate trends in their blood glucose levels**, allowing them to adjust their food or medication intake according activities for instance

Source: glucowise

The Taltz® injection device exemplifies a prefilled syringe, which is not smart, but enhances the ease of use for patients with haptics and sounds



- The medication contained in **Taltz** is used to treat **psoriasis** and certain types of **arthritis**
- The injector is designed to gives patients **clear visual** and **auditory feedback via simple icons, bright colors, translucent material, and clicking sounds**

Source: Taltz

Timesulin® is not smart on its own, but makes conventional insulin pens smarter by displaying the time-span after the last injection

- When the injection is due, the cap can be removed and the injection can start
- Once this procedure is finished, a reset mechanism is triggered the timer

Source: Timesulin

YPSOMED's SmartPilot® turns a conventional autoinjector into a fully connected smart device

- The conventional autoinjector is coupled with the Smart injector allowing to get information on drug **identity, batch number** and **expiry date**
- Once the injection is performed, data is **automatically transmitted to the smartphone** as well as to the relevant HCPs
- After the injection is process is finished, the conventional autoinjectors can be removed and the SmartPilot® is ready for refilling

Source: YPOSEMD

The InPen® by Companion Medical illustrates a further advancement of previous pens allowing to actively control injections and insulin left

Dose Calculator & automatic reminders

- The application incorporates a dose calculator
- The app recommends a personalized dose based on the current glucose level and carbs level

Visualization & sharing of data

- Meanwhile, the pen tracks the current insulin level
- At any time, it can be checked how much insulin is still active after the last dose
- InPen also visualizes how meals and insulin affect meals in order to make informed adjustments

Source: InPen

The Omnipod® system manages the glucose levels in the body through a constant supply of insulin when necessary

Step 1. Fill the Pod.

The Pod automatically primes itself and performs a series of safety checks to prepare for insulin delivery.

Step 2. Apply the Pod.

Place your Pod almost anywhere you would give yourself an injection.

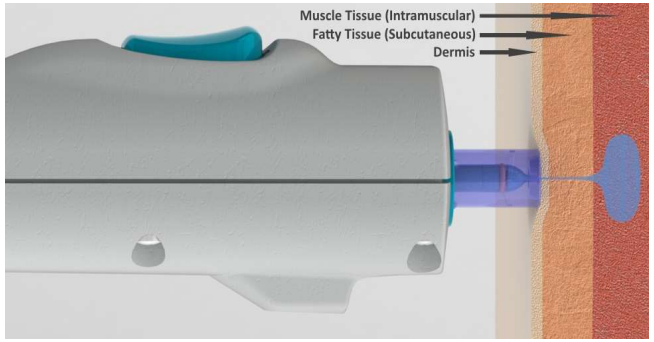
Step 3. Press Start.

The cannula inserts automatically and insulin delivery begins at the touch of a button.

- System **delivers insulin in basal rates**, which refers to **constant supply of insulin** delivered automatically at a personalized, **pre-set rate around the clock**
- The system delivers **additional doses of insulin when needed**, either around mealtime or to correct high blood glucose
- The system itself consists of **a pod and the personal diabetes manager**
- The pod is a **waterproof device**, that **can be filled with insulin** and worn directly on the body. **It includes a small, flexible cannula that automatically inserts insulin**
- The **diabetes manager wirelessly manages the insulin** based on the predefined settings and contains a **built-in glucose meter**

Source: My Omnipod website

Portal Instruments® has brought innovatine advancements into needless jet-injections by controlling the jet of the liquid (drug) at a higher speed



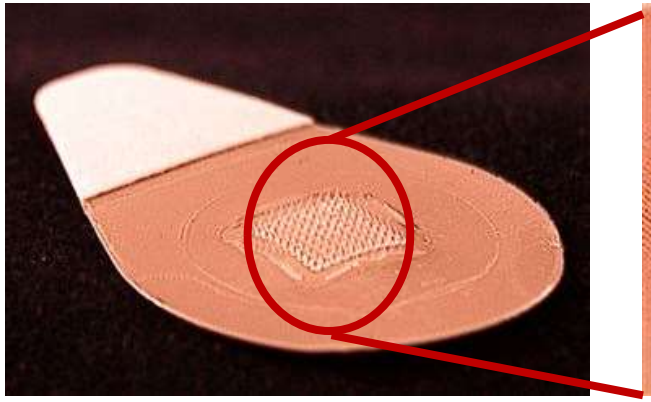
Portal Instruments

- The MIT spinout **Portal Instruments** uses a **jet-injection** method to deliver a **rapid, high-pressure stream of medicine**, as thin as **a strand of hair**, through the skin in adjustable dosages, causing little to no pain
- One of the main advancements (compared to Antares, Endo, Pharmajet, Bioject, etc.) with this delivery system is that **the jet of liquid is more controlled**
- In jet-injector delivery, the stream is exiting the nozzle at **200 meters per second**, or about Mach 0.7
- The device from Portal **uses a closed-loop feedback system** to automatically **adjust the injection velocity** so that it's possible **to target a specific skin depth and location**
- The device can be manually adjusted to accommodate the medication **dosage methodology**, including high-pressure streams where the medication needs to completely breach the skin and lower-pressure injections where the drug is absorbed into the skin's tissue
- The device is designed to work with **hormone treatments, insulin, vaccines, and other drugs with a high-molecular weight**

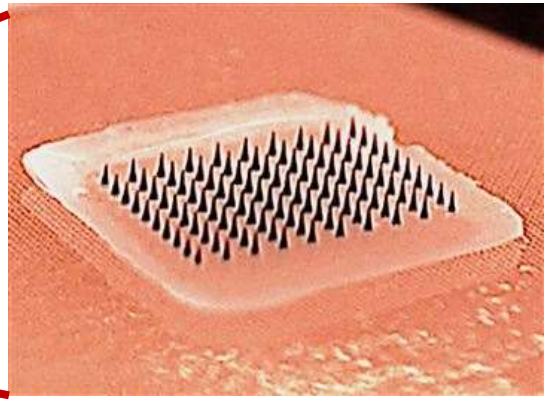
Source: Portal Instruments, Device Plus

Needle-free flu vaccine patch designed by Georgia Tech® founded by Bill & Melinda Gates Foundation

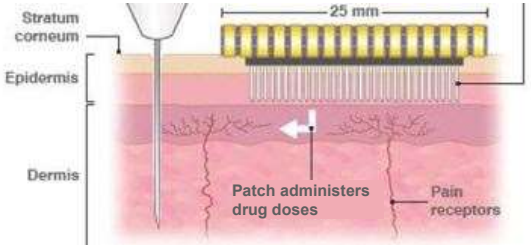
A majority of patients in a study said they would prefer to receive the influenza vaccine using patches rather than traditional hypodermic needles.



This close-up image shows the micro-needle vaccine patch, which contains tiny needles that dissolve into the skin, carrying vaccine



This close-up image shows a microneedle array containing influenza vaccine

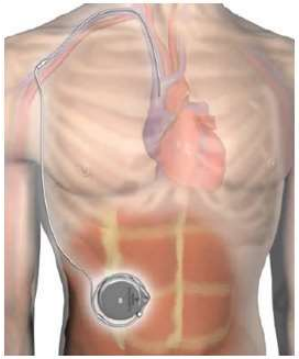


- The team at Georgia Tech®, and a spin-off company called Micron Biomedical®, have been working on the patch vaccine for years
- The microneedle patches were used in a study to see if they would work as well as an old-fashioned flu shot with no serious side effects and without pain
- People who tried out the patch said it was **not difficult or painful to use**, and tests of their **blood suggested the vaccine it delivers created about the same immune response as a regular flu shot**
- These results provide evidence that microneedle patch vaccination is **an innovative new approach** with the potential **to improve current vaccination coverage** and reduce immunization costs

Source: Georgia Tech, News Center

Medtronics®'s system for Remodulin is implanted and delivers the drug through the vein

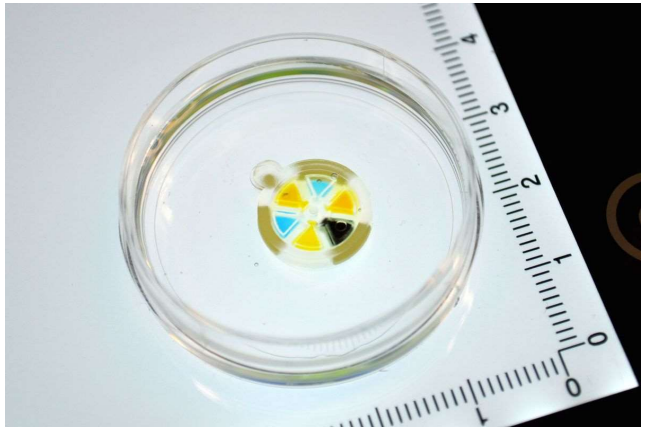
Implantation

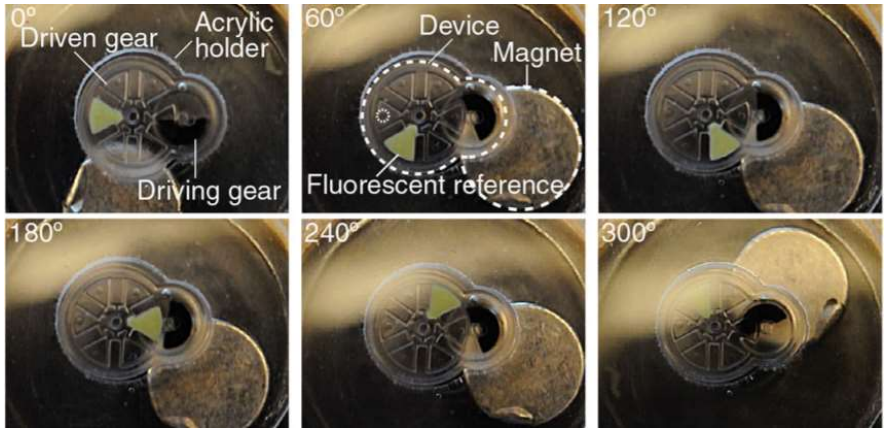


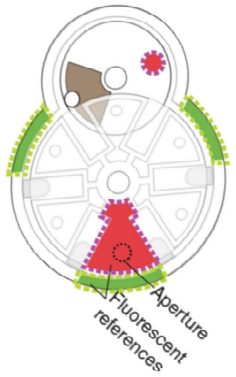
- **The Implantable System** for **Remodulin** is an infusion system that is fully implanted into a patient **to deliver Remodulin through a patient's veins**
- Remodulin (or Treprostinil) is a medication used to treat **Pulmonary Hypertension**
- **Surgeons insert the intravascular catheter through a vein at the superior caval-atrial junction** (the joint between the superior vena cava and the heart) and **connect the catheter to the pump in a pump pocket placed beneath the abdominal skin**
- The pump remains **permanently implanted** and the health care provider **uses a needle and syringe to refill** the pump with Remodulin as needed

Source: FDA website

Columbia University scientists have develloped a biobot implanted under the skin, releasing the drug in the tumor area







- A **biobot that can be implanted under the skin and deliver doses of drugs; size 5mm**
- The **3D-printed micromachine** has **no batteries or wires**, but is **activated through an external magnet**
- The **biobot** is made of **hydrogel** that makes the machine **soft but resistant**
- **Mechanism of action**→ In this hydrogel biobot, the Geneva drive is activated by an external magnet; **the rotation allows one of six tiny chambers filled with drugs to line up with a hole and release a dose**
- When **implanted under the skin** in the tumor's area, a doctor could simply use an outside magnet **to move the gear** and **deliver the drug when needed**

Source: The Verge; Yin Chin et al.

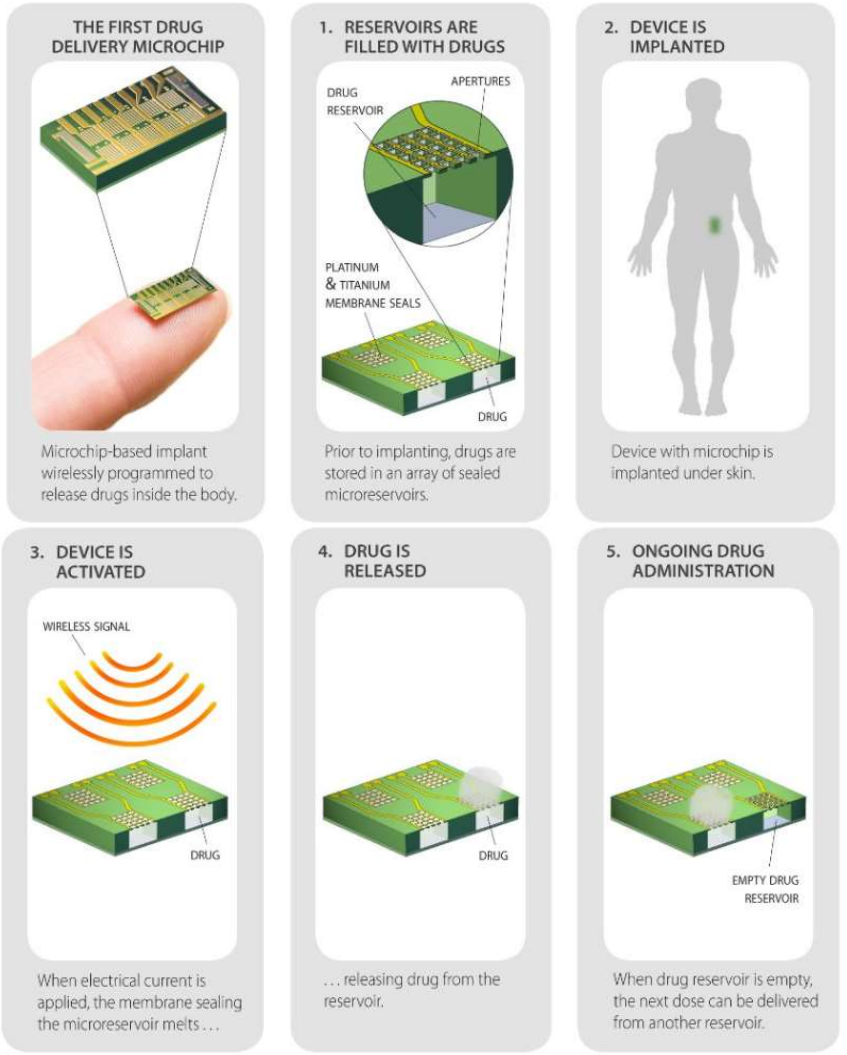
Microchips can be implanted and release periodically the drug in the patient´s body and it can remotely be switched on or off

Prevention without substantial patient interaction

- The implant contains a dose of a **contraceptive sufficient for 16 years**
- Device **releases** 30 µg of the contraceptive every day
- The drug is stored between **ultra-thin layers** and realeased when a **layer dissolves** as a rection to an **electrical current**
- Patients can **turn the device on and off remotely**

microchips
programmable drug delivery

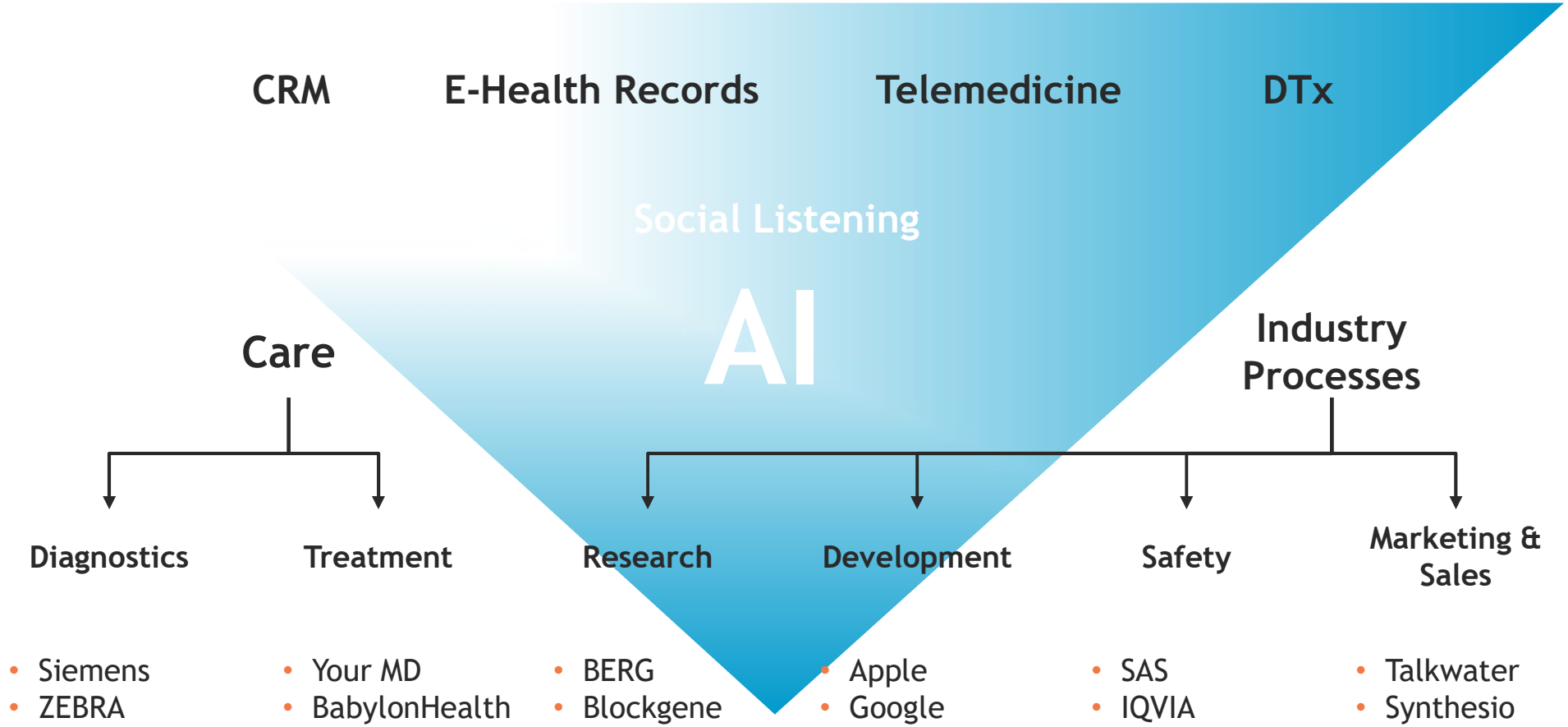
- The product is designed to **hold any other drug** to be administred that way



Source: Microchips

AI provides breakthrough solutions for unmet needs, for each costumer and for the industry itself

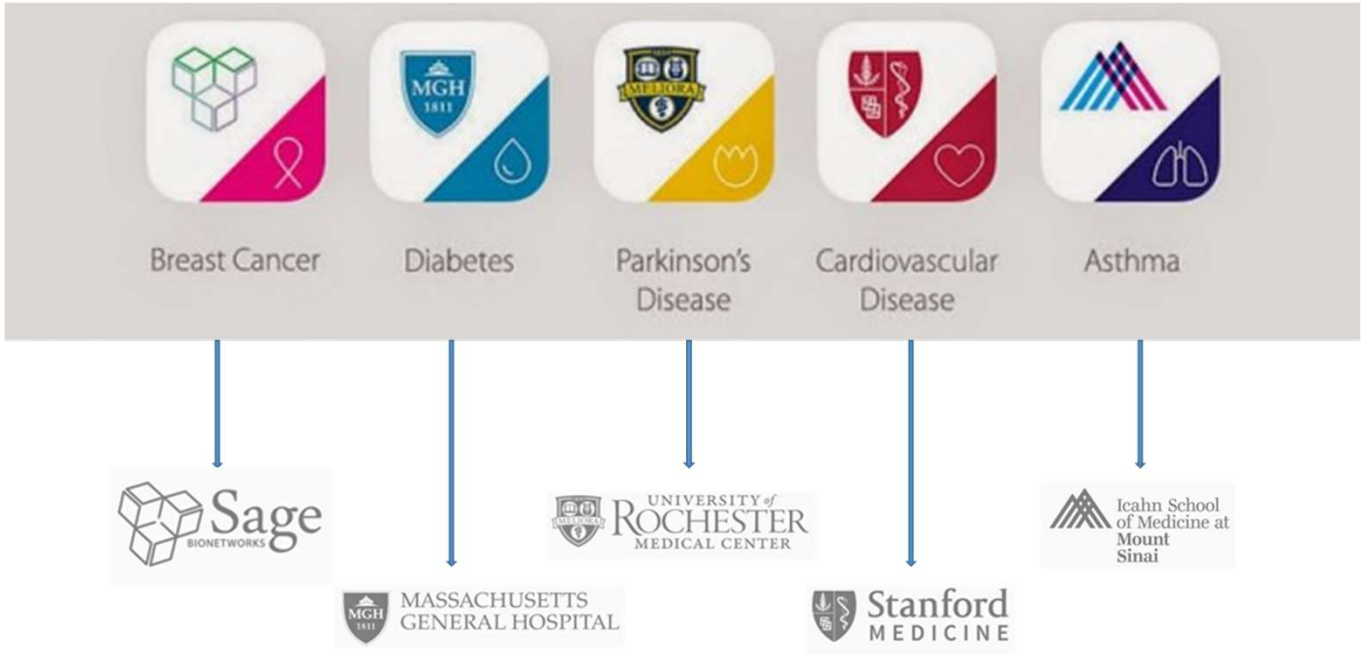
Digitalization in Healthcare



Source: stradoo

mHealth has the potential to revolutionize research by generating a huge and cost-free mass of important patient data

The Apple Research Kit uses the iPhones functions to generate research data from patients



Apple Research includes Apps which generates research data from patients

- Symptoms, courses of a disease, therapies and after care for several diseases are collected and evaluated by researchers
- Data is collected with Apple products like the iPhone or the iWatch and Apps like the Apple Health apps

Source: Apple

Survivors of diseases are a valuable source of information which can be easily accessed with the help of mHealth

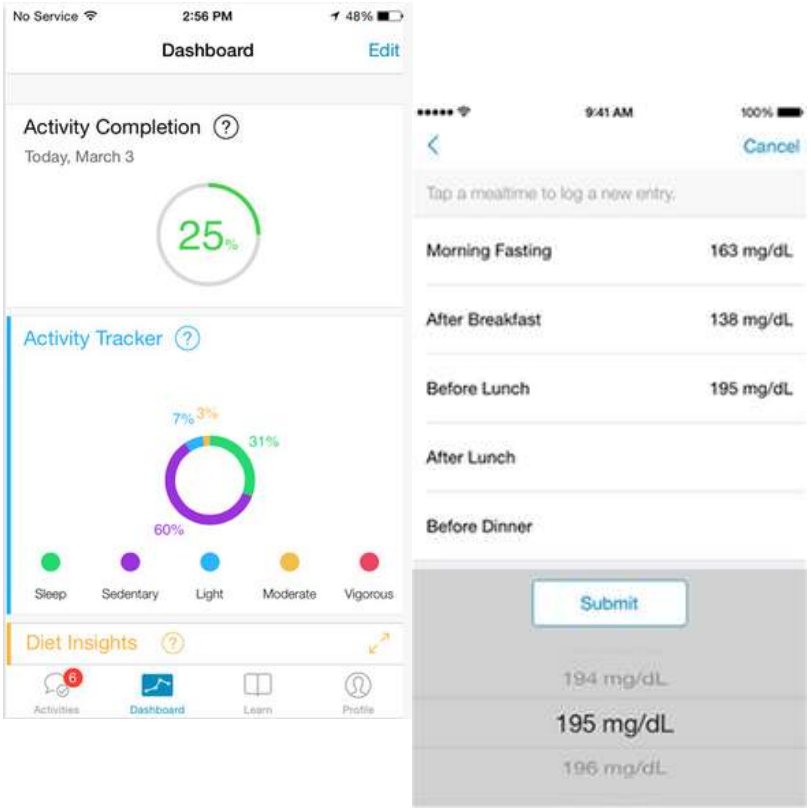
Share the Journey collects data from breast cancer survivors

- **Aim:** Understand symptoms after breast cancer treatment
- Using questionnaires and collection of phone sensor data to track fatigue, mood and cognitive changes, sleep disturbances, and changes in exercise
- Key Features:
  - Recording and tracking of daily symptom variations
  - Sharing of insights and partnering with researchers
  - Education about breast cancer treatment and symptoms
  - Importing daily physical activity measurements from the Apple Health app

Source: Share the Journey

mHealth can be used to collect data about how the individual lifestyle influences the patients health situation

Gluco Success helps researchers to understand how daily life influences diabetics

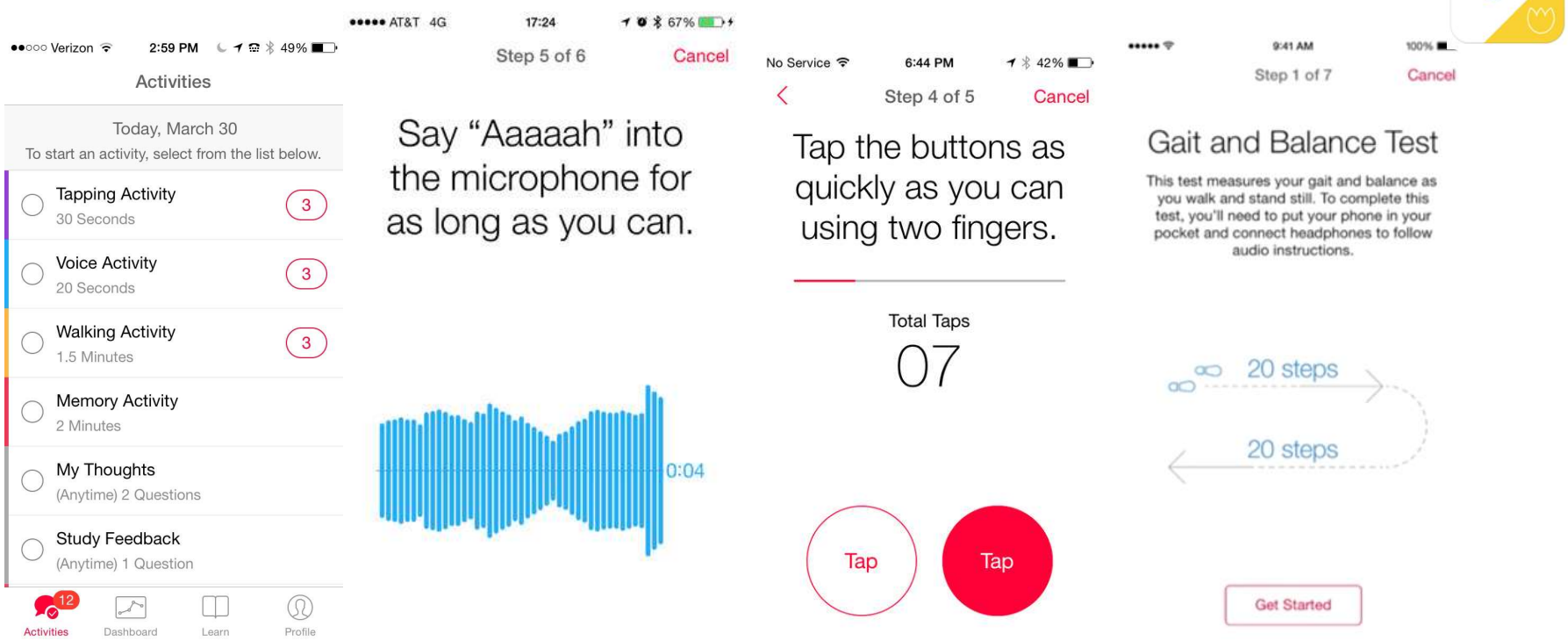


- **Aim:** Understand how health behaviours influence blood glucose in real life
- Data taken from the Health Kit
  - Height and Weight
  - Blood glucose
  - Carbohydrates
  - Dietary calories and sugar
  - Steps
  - Biological sex
  - Tracking physical activity automatically by the iPhone's accelerometer
  - Connection with "Lose it app" gains data about diet

Source: Gluco Sucess

Quick and simple tasks collect data about the course of disease of chronically ill people

Parkinson mPower collects data by letting participants fulfill easy ans short tasks

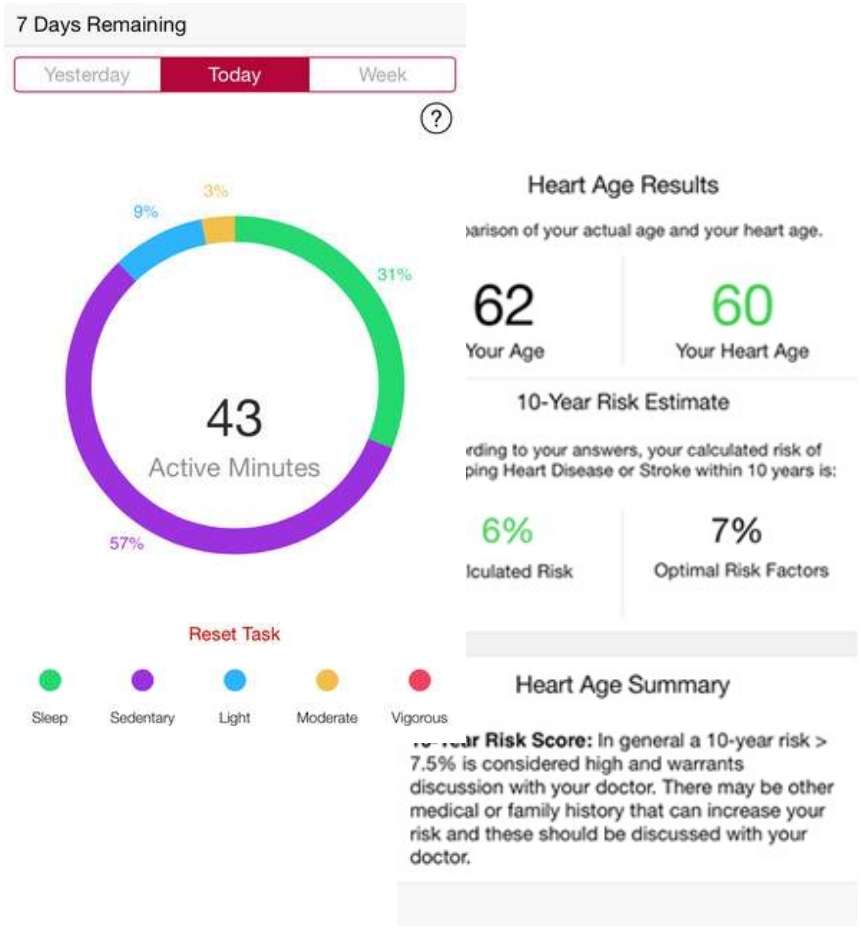


- **Aim:** Collect data from patients with Parkinson‘s
- Patients have to fulfill easy tasks at different times to collect data about the memory, the fine coordination of motor behavior and manual skills

Source: Parkinson's mPower

MyHeart Counts® combines research with education and thereby gain a profit for all sides

MyHeart Counts helps users to understand the importance of a healthy cardio vascular system



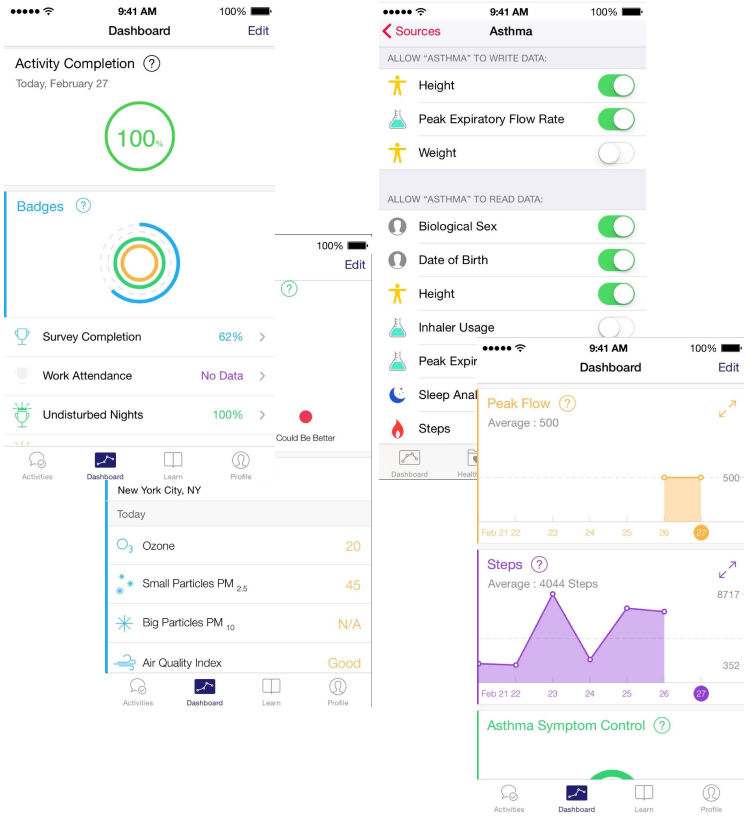
Aim: Improving the understanding of heart health

- Recording and tracking of physical activity through iPhone or a Apple Health App-linked device
- Analysing the fitness level, through a 6 minute walk test
- Reminders and notifications about activity and sleep
- Surveys on Physical Activity Readiness and other health factors
- Entering blood pressure and cholesterol levels to calculate risk score
- Education about:
  - Activity level and walking fitness
  - Risk factors and how to improve
  - Heart disease and stroke
  - Heart age

Source: My Heart Counts

Asthma Health® can combine data from the smartphone with data collected by the patient in order to monitor how health situations change

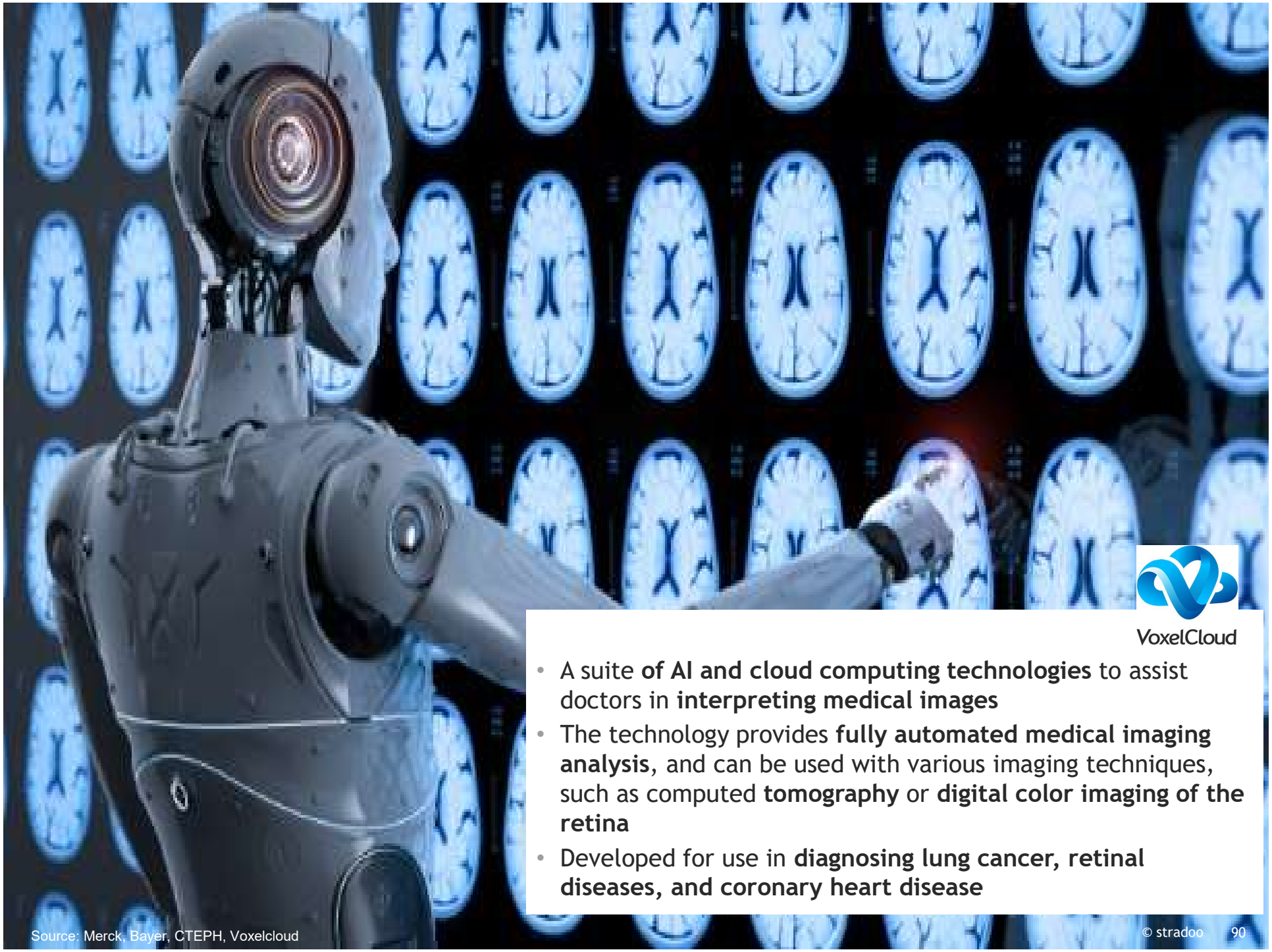
Asthma Health collect data from Asthmatics in order to support the research



Aim: Gaining greater insight into asthma

- Recording and tracking of day- and night-time asthma symptoms and their affection on daily activities
- Recording usage of controller and rescue inhalers
- Triggers colds, increased physical activity, strong smells, exhaust fumes, house dust and animals
- Emergency department visits, medical visits, and changes in medication
- Physical activity through Apple Health Kit enabled devices
- Reminders and notifications about medications and local air quality
- Education:
  - ➢ Proper inhaler technique
  - ➢ Watch physician-approved videos for tips on effective asthma management

Source: Asthma Health



VoxelCloud

- A suite **of AI and cloud computing technologies** to assist doctors in **interpreting medical images**
- The technology provides **fully automated medical imaging analysis**, and can be used with various imaging techniques, such as computed **tomography** or **digital color imaging of the retina**
- Developed for use in **diagnosing lung cancer, retinal diseases, and coronary heart disease**

Source: Merck, Bayer, CTEPH, Voxelcloud

Enlitic® uses deep learning to analyze unstructured medical data to give doctors better insights about patients needs

Triage

Their models **interpret scans** as they are acquired, enabling a radiologist to prioritize their worklist based on the findings in each study

Real Time Support

Their **models read studies alongside radiologists**, **detecting rare and subtle findings**, providing **measurements and descriptions**, automating longitudinal analysis, and even **generating reports**

Quality Assessment

Their models can provide **a post-read analysis**, **checking a radiology report against the corresponding images** to help prevent over or under-called findings

Source: Enlitic website

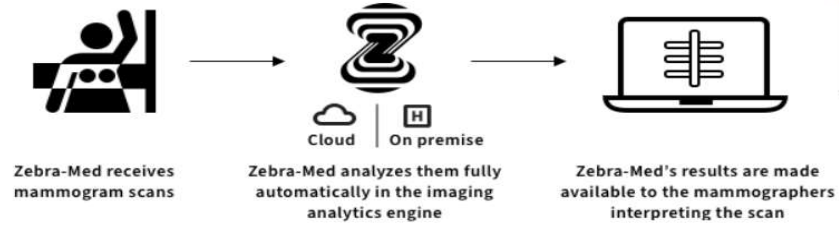
Zebra Medical Vision® uses an AI to help radiologist make better diagnosis

Automatically analyzes imaging scans from various modalities for a number of different clinical findings

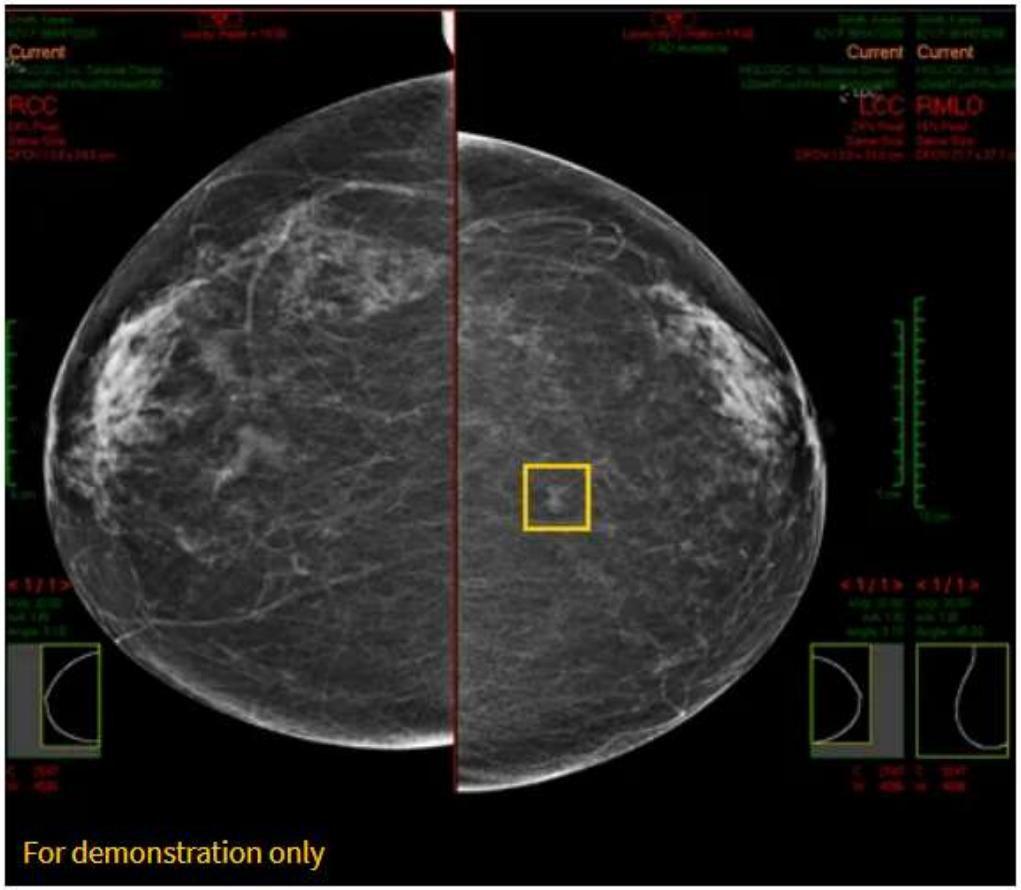
Zebra-Med uses a proprietary database of **millions of imaging scans**, along with **machine and deep learning tools**, to create software that analyzes data in real time with human level accuracy

The Triage Mammography product then returns its result to the radiologist workstation, either by signaling within the worklist or alert

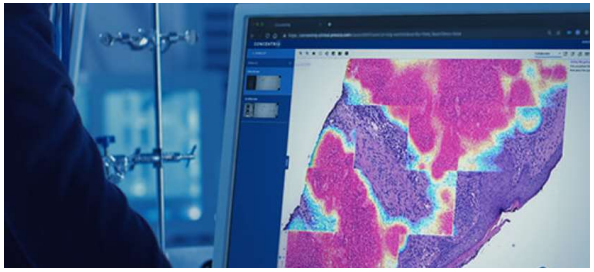
Zebra Engine uncovers **brain, lung, liver, cardiovascular and bone disease in CT**

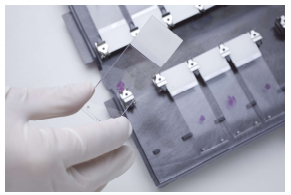


Source: Zebra website



Proscia® uses a digital pathology platform where the AI is able to “read” images, detect patterns that supports cancer discovery and treatment





- Proscia is a **digital pathology** platform that uses AI **to detect patterns in cancer cells**
- The company’s software **Concentriq®** helps pathology labs eliminate bottlenecks in data management and uses **AI-powered image analysis** to connect data points that support **cancer discovery and treatment**

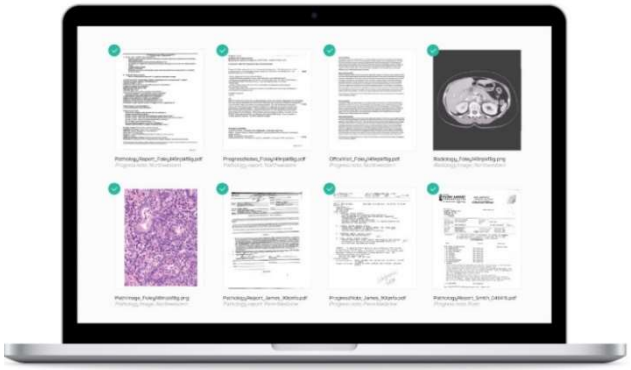
- Concentriq® is the leading software platform for digital and computational pathology. It can **“read” a whole slide image** and **apply specialized algorithms** that can perform many useful clinical tasks to augment the role of the pathologist

- The AI software can **auto-categorize tissue samples** by **disease state** and then route them to specific pathologists for review

Source: Proscia website

Tempus – a modern unicorn - is using AI to combine data from genetic sequencing and image recognition for finding better patient treatment

TEMPUS



GENERATE GENOMIC RESULTS	Their genomic tests **analyze DNA, RNA**, and **proteomic data to understand a patient's tumor** at the **molecular level**
TRANSFORM UNSTRUCTURED DATA	They **ingest and organize clinical notes, lab reports, pathology images, and radiology scans to capture phenotypic, therapeutic, and outcomes data** to understand the **clinical context** for each patient case
DELIVER ACTIONABLE INSIGHTS	Their platform analyzes thousands of clinical and **molecular data points**, **connecting physicians with up-to-date treatment options** and relevant insights for patients based on their **unique molecular profile** and their **advanced analytics** and **machine-learning algorithms**

Source: Tempus

Vicarious Surgical miniaturized robotics put motion into the abdominal cavity from far distance

- Vicarious Surgical **combines virtual reality with AI-enabled robots** so surgeons can perform **minimally invasive operations.** Using the company's technology, surgeons can virtually **shrink and explore the inside of a patient's body** in much more detail.

- Using the motorized robot **a surgeon can remotely control the robot's movements** to **operate on a patient**
- **Two robotic arms** that have the **same degrees of freedom and proportions** of a human arms and **a camera** that is placed above the shoulders of the robot
- **Surgeons look through the "eyes" of the robot** and can look down and see the robot's arms.
- The robot tracts the surgeon's arm motion and mimics their arms and hands

Source: Vicarious Surgical website, Techcrunch

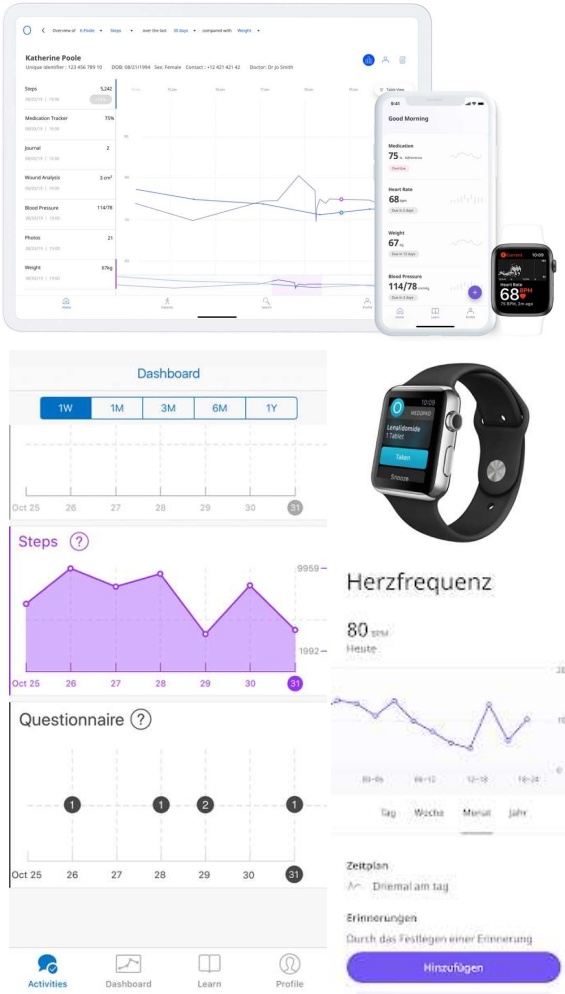
Medopad® has specialized in remote patient monitoring for patients with rare and chronic diseases and is focused in finding “digital biomarkers”

medopad → HUMA

Total funding amount: $54M

Digital health business Medopad has rebranded itself as Huma

Acquired two AI and wearable tech companies, reinforcing its mission to play a pioneering role in discovering **digital biomarkers**



- Medopad (Huma) uses machine learning and big data analyses to help **predict and manage chronic diseases**
- Patients use an AI powered **mobile app to track and monitor their symptoms**

- **The app can:**
  - Monitor the vital signs when outside the hospital so the patient and the doctor can understand how the patients is feeling
  - Log symptoms so the patient has a record that can discuss with his/her care team
  - Improve drug adherence by helping set medication reminders
  - To better understand personal healthcare through educational materials

- The app will ask users to participate in a **number of online tests (questionaires)**, such as **performing hand movements in front of their phone’s camera** that help doctors **gather information** on the development of the patient´s condition

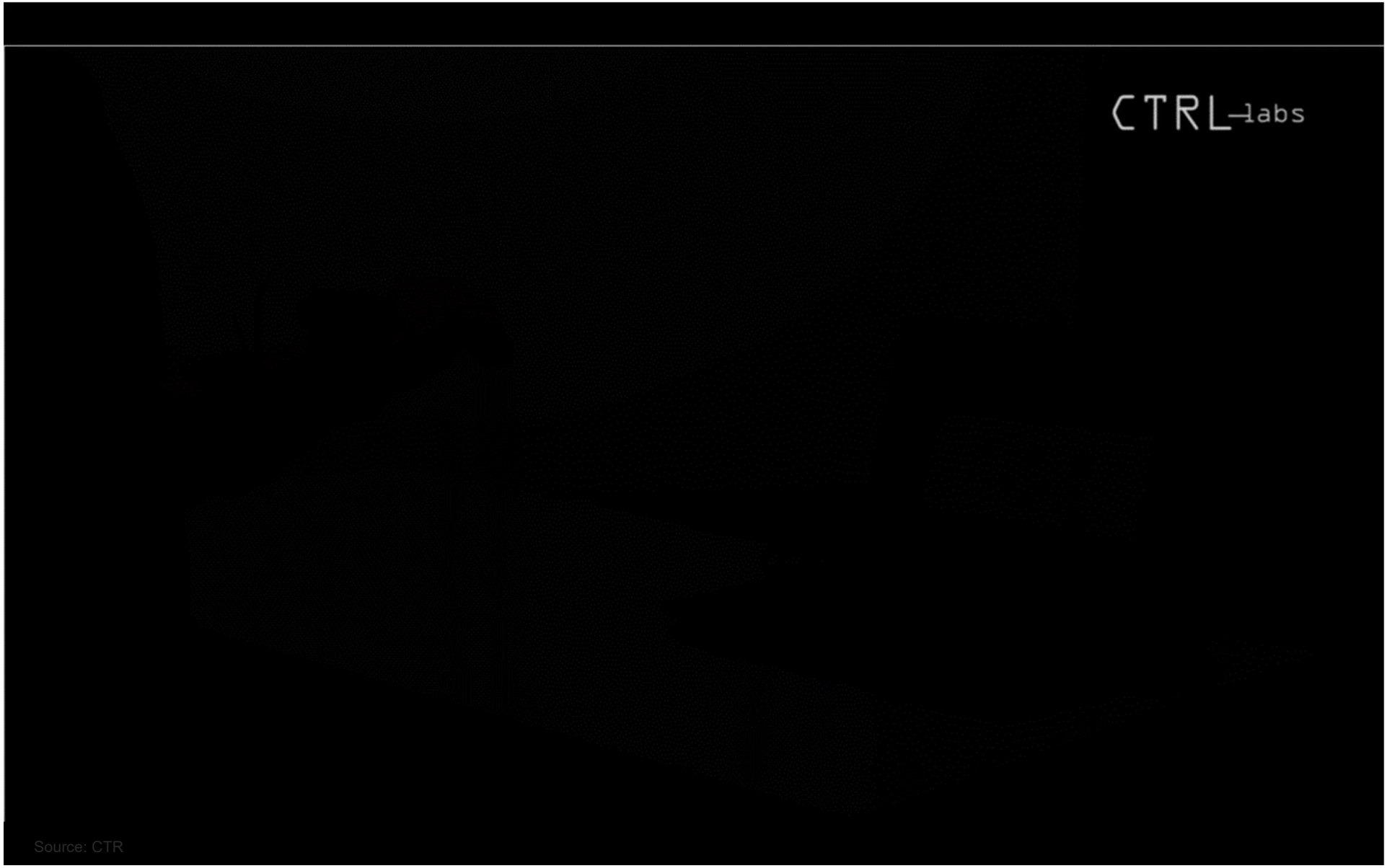
- **Combined, wearables and connected devices** create an incredible amount of data about individuals, with data points known as **digital biomarkers** which Medopad (Huma) uses to **predict health-related outcomes**

Source: Medopad website, Crunchbase

CTRL-kit is using neuronal signals to steer any kind of hardware or even to control a medical prothesis

- A ‘neural controller,’ which uses the **electrical activity produced by muscles** and employs those signals as a type of **gestural controller for interacting with computer applications**
- The kit uses differential **electromyography** to translate electrical pulses into actions by measuring changes to the electric potential from **signals sent by the brain to the user’s hand muscles**
- The controller uses electrodes to monitor these signals and converts them by using a **machine-learning algorithm** to **distinguish the individual pulses** of each and turn them into gestures a computer can recognize
- It also supports the integration with **VR and AR** applications

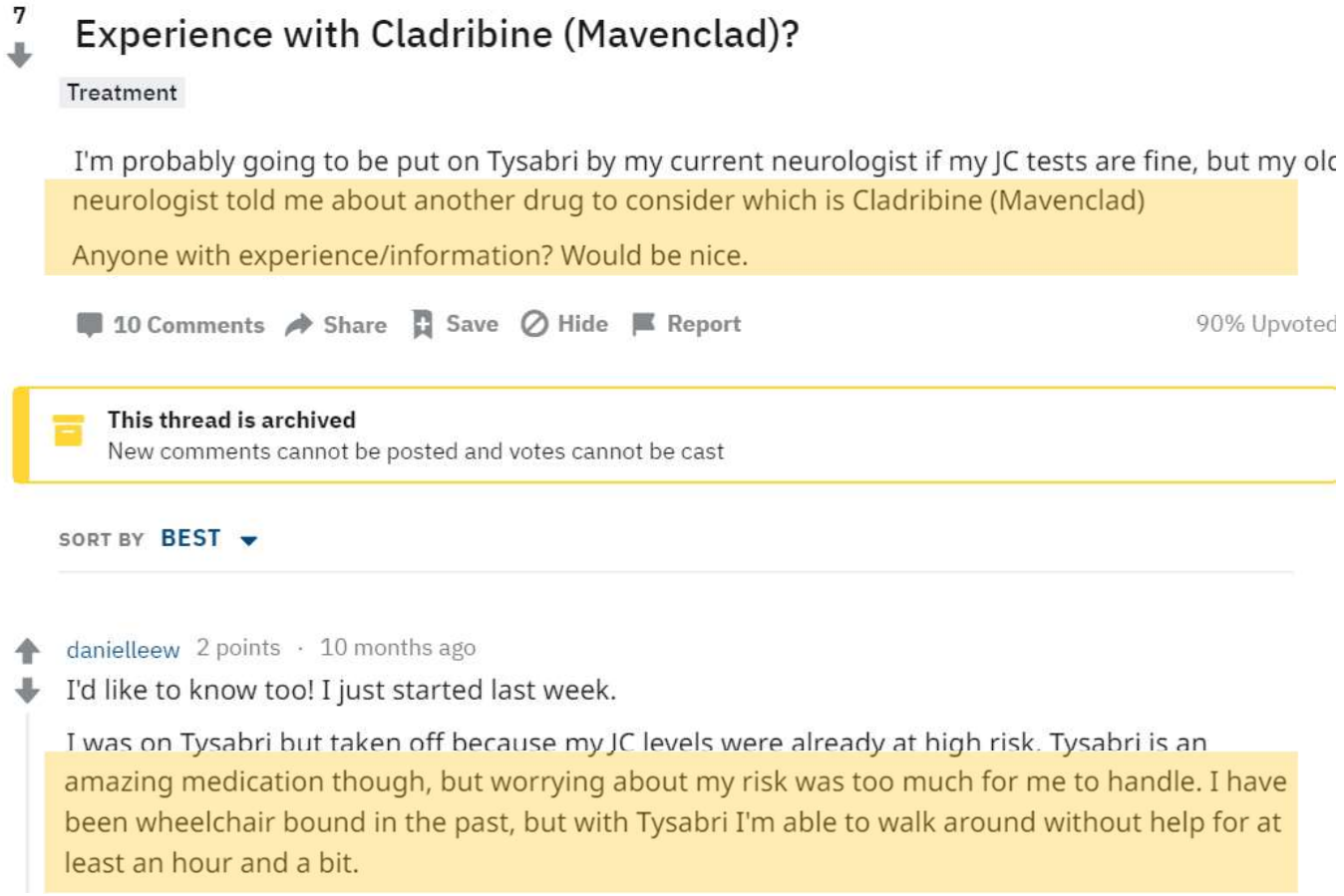
Source: CTRL-kit website



Source: CTR

Do you know what your patients are talking - unbiased in the www -it could be promotion or serious side effect

Excerpt from Reedit Mavenclad disussion



Source: stradoo, Reedit

Synthesio's Social Listening can help you make sense of all of your online data and turn it into strategic and actionable insights for your business

The Synthesio Social Intelligence Suite gathers data from the largest collection of social and mainstream web sources

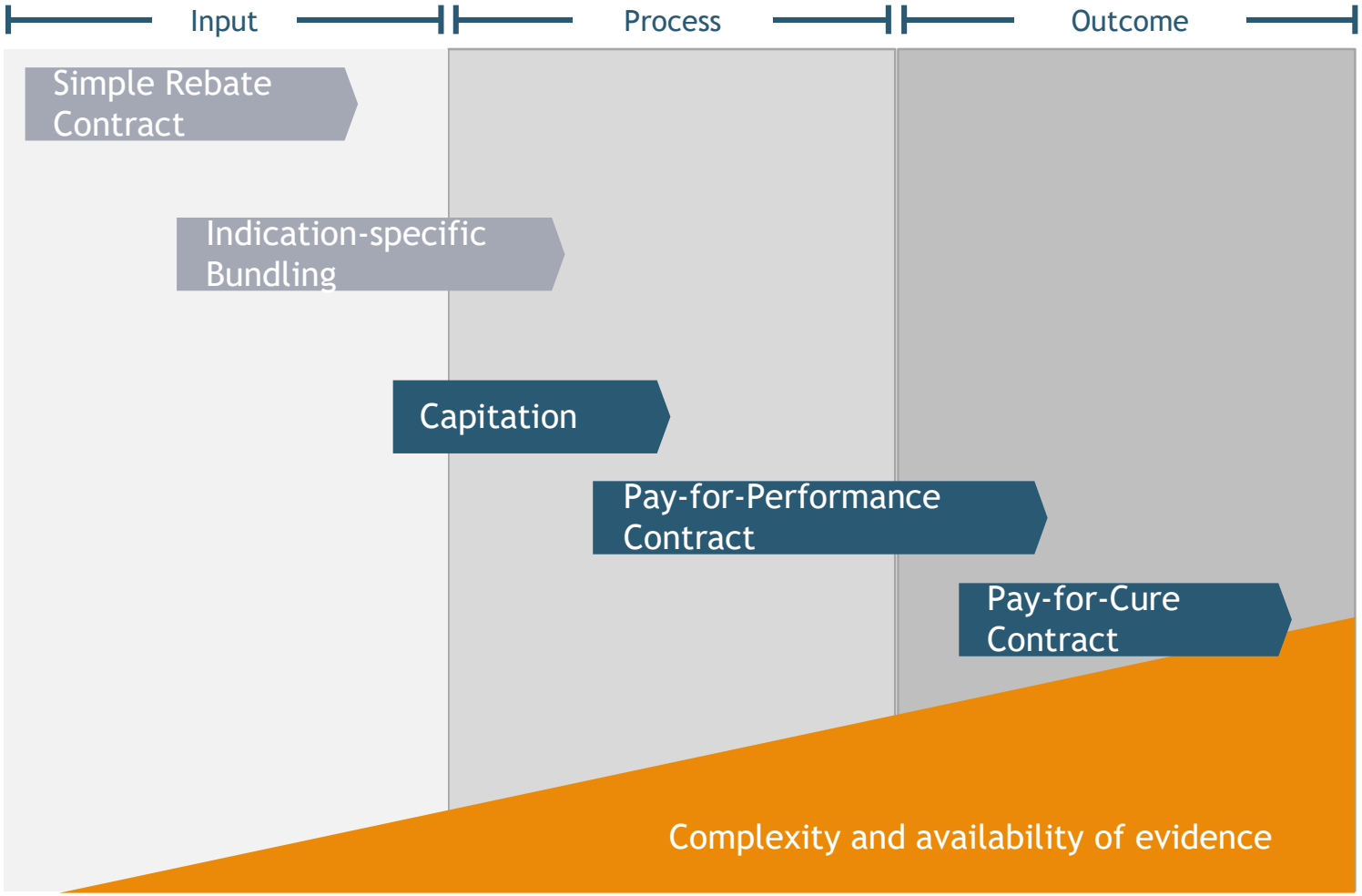
Source: Synthesio

Payors will have to adapt to the new paradigms


IF I KILL YOU,
YOU DON'T
PAY
DR. NICK RIVIERA

Agreements have to be built from financial, outcome and service components

Contract development & component of risk sharing agreements



Source: Pharmaceutical Executive, stradoo

Sharing risk may apply to price reductions, volume caps or even total re-pays in case of therapy failures

Fixed budget agreement (Australia)

Enbrel (Wyeth/Pfizer)
Rheumatoid Arthritis
Pharmaceutical Benefits Pricing Authority (PBAC)

No-cure, no-pay deal (Germany)

Aclasta (Novartis) Osteoporosis
DAK and Barmer Ersatzkasse

Performance based payment

Velcade (Johnson & Johnson)
Multiple Myeloma
National Health Service (NHS)

Criteria

Patients have to **show clinical response every three months** (based on rheumatoid factor) in order to continue reimbursement
If **annual spending** for the scheme **exceed A$100 million, Pfizer covers additional costs**

Novartis **funds the cost** of its drug in cases **patient experiences an** osteoporotic fracture within 1 year following drug infusion

NHS pays for the drug **only if** tumor shrinks and **50% reduction in blood serum M-protein levels** prove positive effect

Source: press research

In almost all countries payers have began to use risk-sharing

Overview of selected risk-sharing agreements

	Company	Indication	Criteria	Price		Performance	
				Cost caps	Rebate	Monitor	Compliance
	Sutent (sunitinib malate) Pfizer	Kidney Cancer	**50% discount** if used in the first two or three treatment cycles	x	✓	x	x
	Tarceva Roche	NSCLC[1]	**50% discount** if used in the first two or three treatment cycles	x	✓	x	x
	Nexavar (sorafenib) tablets Bayer	Renal cancer	**50% discount** treatment cycle				
	SPRYCEL BMS	CML[2] / ALL[3]	**50% discount non-responde**				
	Januvia / Janumet Merck	Diabetes	**Discounts inc** certain blood-s if patient **takes**				
	LUCENTIS RANIBIZUMAB INJECTION Novartis	Wet AMD[4]	NHS pays for 1 **for further inje**				
	Yondelis Pharma Mar	Soft tissue sarcoma	**NHS pays for** further cycles p				
	Enbrel etanercept Pfizer	Rheumatoid arthritis	**Restricted acc** Pfizer pays for **A$100 million**				

	Company	Indication	Criteria	Price		Performance	
				Cost caps	Rebate	Monitor	Compliance
	myfortic / CERTICAN / SANDIMMUN Optoral Novartis	Kidney transplants	**Full re-payment** of cost of medicine **if treatment fails**	x	✓	✓	x
	aclasta zoledronic acid Novartis	Osteoporosis	**Full re-payment** of cost of medicine **if treatment fails**	x	✓	✓	x
	aclasta zoledronic acid Novartis	Osteoporosis	In case of treatment failure **full re-payment of drug and associated treatment costs**	x	✓	✓	x
	Nexavar (sorafenib) tablets Bayer	Liver cancer	**Full compensation for costs of treatment failures** after the first treatment cycle	x	✓	✓	x
	Tasigna Novartis	Leukemia	**Full compensation for costs of treatment failures** after the first treatment cycle	x	✓	✓	x
	PROSCAR Merck Frosst	BPH[1]	**Repay** full cost if patients **require surgery after 1 year** of therapy	x	✓	✓	✓
	Actonel P&G / Sanofi	Osteoporosis	Companies **cover costs induced by treatment failure**	x	(✓)	✓	✓
	Tracleer Actelion	IPAH	**Limiting treatment failures** by **restricting access** to eligible patients	x	x	✓	x
	Enbrel etanercept Pfizer	Rheumatoid arthritis	**Pfizer funds and provides compliance support** to patients;	x	x	x	✓

Source: Press research 1) Non small cell lung cancer 2) Chronic myeloid leukemia 3) Acute lymphoblastic leukemia 4) Wet age-related macular degeneration

There are various examples digital therapeutics that have been added to coverage plans

Sleepio

- Automated yet highly personalized **digital therapeutic application for poor sleep**
- BigHealth has entered **partnerships with NHS** which allows their employees to have free access to the application
- Price: 220€ per year

KaiaHealth

- Kaia is **a pain management technology**, that delivers **multimodal mind body therapy for musculoskeletal** disorders
- Price: 80€ per year, but thanks to reimbursement deals with German health insurance companies, it is **available free of charge in Germany**

Freespira

- Freespira is a **digital therapeutic for panic disorder and panic attacks** occurring with other anxiety conditions
- The device was **added to Highmark's medical policy in 2018**
- Price: Around **720-850€**

Source: sleepio, kaiaHelath, Freespira®

Many DTx have ben reimbursed and included in Health Plans already

Examples for reimbursement of DTx

- Big Health's **Sleepio** product receives coverage by the NHS (20 May 2019)
- WellDoc's **BlueStar** product receives coverage by Business Health Care Group (14 May 2019)
  - This HbA1c reduction, according to an economic analysis conducted in partnership with IBM Watson Health, would correspond to the average cost savings of **$254-$271 per user** per month.
- **Omada Health's** product receives coverage by Priority Health (3 October 2018)
- Palo Alto Health Sciences's **Freespira** product receives coverage by Highmark Inc. (24 September 2018)
  - Improved health resulted in **$424 to $972** in net medical cost savings over two years compared to non-participants, equating to a return on investment ranging from 1.5 to 2:1 for employers[1,]
- **Omada Health's** product receives coverage by Cigna (18 September 2018)
- **Propeller Health's** product receives coverage by Anthem Blue Cross and Blue Shield (16 August 2018)
- **Voluntis**' Insulia product receives coverage by WellDyneRx (14 May 2018)
- **Pear** Therapeutics con reset (2018)
- **Propeller Health's** product receives coverage by Express Scripts (16 November 2017)

Source: stradoo, DVG

In targeted therapies, treatment cost have been heavily criticized

Public “distorted” perception of cost-benefit

SPIEGEL

Wissenschaft

GESUNDHEIT

„Schlicht obszön“

Dutzende neuer Krebsmittel drängen auf den Markt. Die Verheißung ist gewaltig, der Nutzen jedoch fraglich – nur die Hersteller profitieren. Jetzt wehren sich Ärzte. Denn die astronomischen Preise dieser Präparate gefährden das Gesundheitssystem.

Avastin
Roche, Schweiz

JAHRES-THERAPIEKOSTEN
55 714 €

LEBENSVERLÄNGERUNG IN MONATEN
Durchschnitt im Vergleich zur Standardtherapie

bei Lungenkrebs:	**2,0** (12,3 statt 10,3)
bei Darmkrebs:	**4,7** (20,3 statt 15,6)
bei Brustkrebs:	**5,6** (11,4 statt 5,8)*
bei Nierenkrebs:	**4,8** (10,2 statt 5,4)*

Nexavar
Bayer, Deutschland

JAHRES-THERAPIEKOSTEN
58 400 €

LEBENSVERLÄNGERUNG IN MONATEN
Durchschnitt im Vergleich zur Standardtherapie

bei Leberzellkarzinom:	**2,8** (10,7 statt 7,9)
bei Nierenzellkarzinom:	**3,4** (19,3 statt 15,9)

Tarceva
Roche, Schweiz

JAHRES-THERAPIEKOSTEN
29 525 €

LEBENSVERLÄNGERUNG IN MONATEN
Durchschnitt im Vergleich zur Standardtherapie

bei Lungenkrebs:	**2,0** (6,7 statt 4,7)
bei Magenkrebs:	**0,8** (5,9 statt 5,1)

Herceptin
Roche, Schweiz

JAHRES-THERAPIEKOSTEN
39 394 €

LEBENSVERLÄNGERUNG IN MONATEN
Durchschnitt im Vergleich zur Standardtherapie

bei Brustkrebs:	**7,0** (25 statt 18)
bei Magenkrebs:	**4,2** (16 statt 11,8)

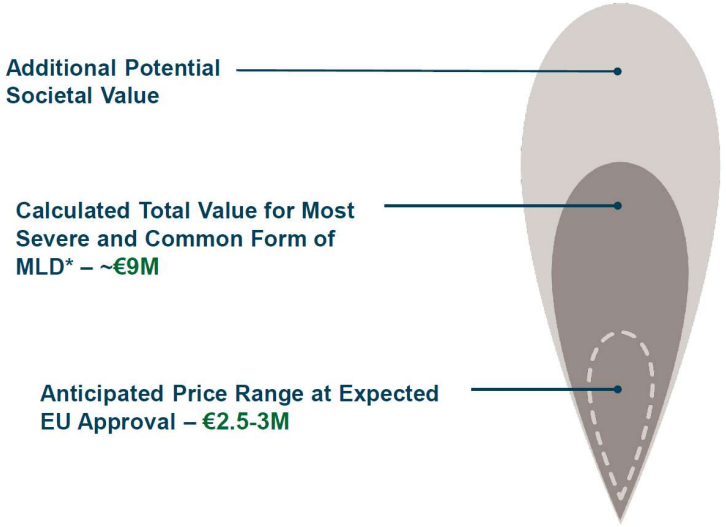
Source: Der Spiegel 20 / 2010 auf Basis des Ludwig Boltzmann Institut für HTA und Ulrich Schwabe

Cell and gene therapies are revolutionizing the field of medicine by offering life-changing benefits

- Therapies have been gaining considerable attention recently, both for addressing **long-standing unmet needs** and for **being exceptionally pricey**
- **Prices** get their orientation from relevance of unmet need, burden of disease and cost of therapies saved
  - Spark Therapeutics' **Luxturna,** a gene therapy for congenital amaurosis, a rare eye disease - **($425,000)**
  - Gilead's CAR-T drug, **Yescarta,** a cancer therapy for adults with relapsed or refractory large B-cell lymphoma - **($373,000)**
  - Novartis' CAR-T product, **Kymriah,** a cancer therapy for patients up to age 25 with cancer B-cell precursor acute lymphoblastic leukemia and adults with relapsed or refractory large B-cell lymphoma - **($475,000)**
  - Biogen's **Spinraza,** a therapy for **spinal muscular atrophy ($375,000 - $750,000)**
  - Novartis's **Zolgensma,** a gene therapy for **spinal muscular atrophy - ($2.1 million)**

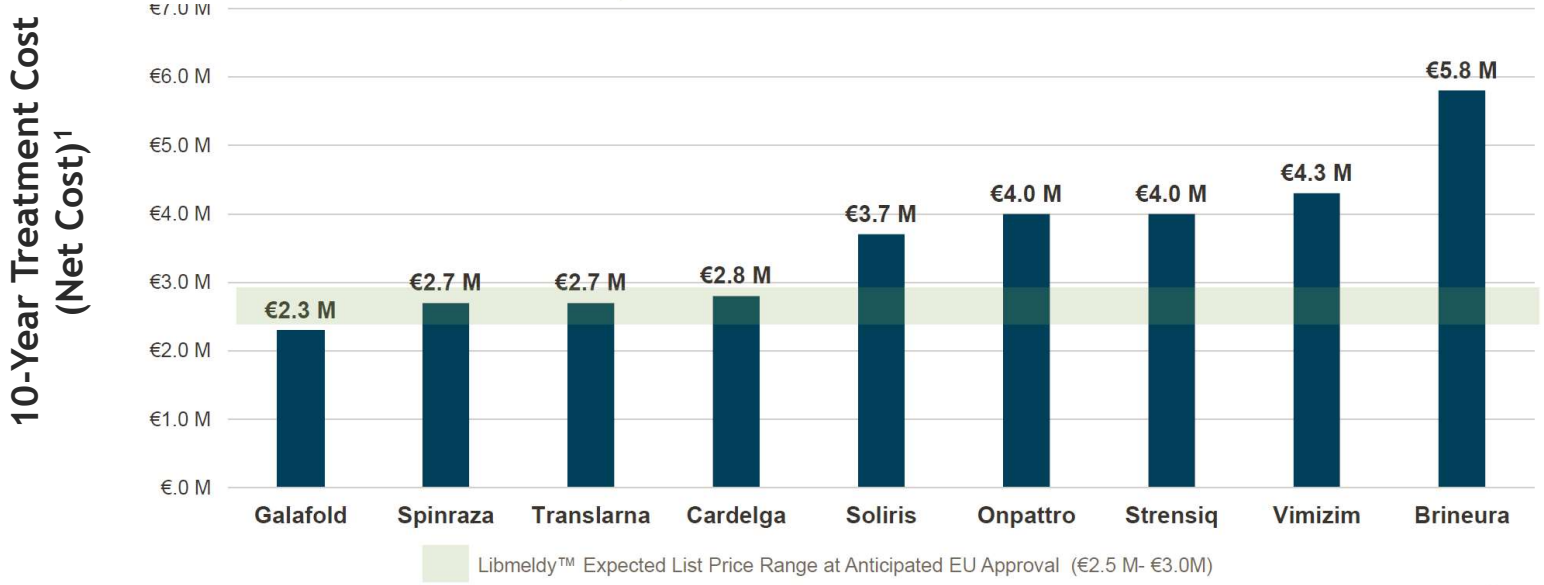
Source: https://decisionresourcesgroup.com/blog/cell-gene-therapies-five-key-access-reimbursement-strategies/

Estimated Libmeldy™ Value vs. Anticipated Price Range - costs less than most chronic rare disease therapies over 10 Years



Orchard Pricing Commitments

- Shared Value
- Shared Risk
- Informed Pricing
- System Wide Evolution



Source: Orchard Therapeutics Corporate Presentation, Aug 2020

Valuations give an indication of hope and promise coming from AI and DTx

Pear THERAPEUTICS

...received a funding of **$135 m**

flatiron

... market cap at **$2 bn**

babylon

...was sold for **$1.9 bn** to **Roche**

...received a funding of **$60 m**

zebra MEDICAL.VISION

TEMPUS

...received a funding of **$620 m**

...was sold for **$100 m** to **Roche**

mySugr

Source: press releases

...outlook to 2035

…in 2035

- Personalized medicine has become state of the art – many treatments are not drug-based anymore
- Stem cells are cultivated by new players in the industry, allowing to grow what ever tissue is needed
- Adherence measures have become routine, resulting in a multitude of new devices and technologies

…in 2035

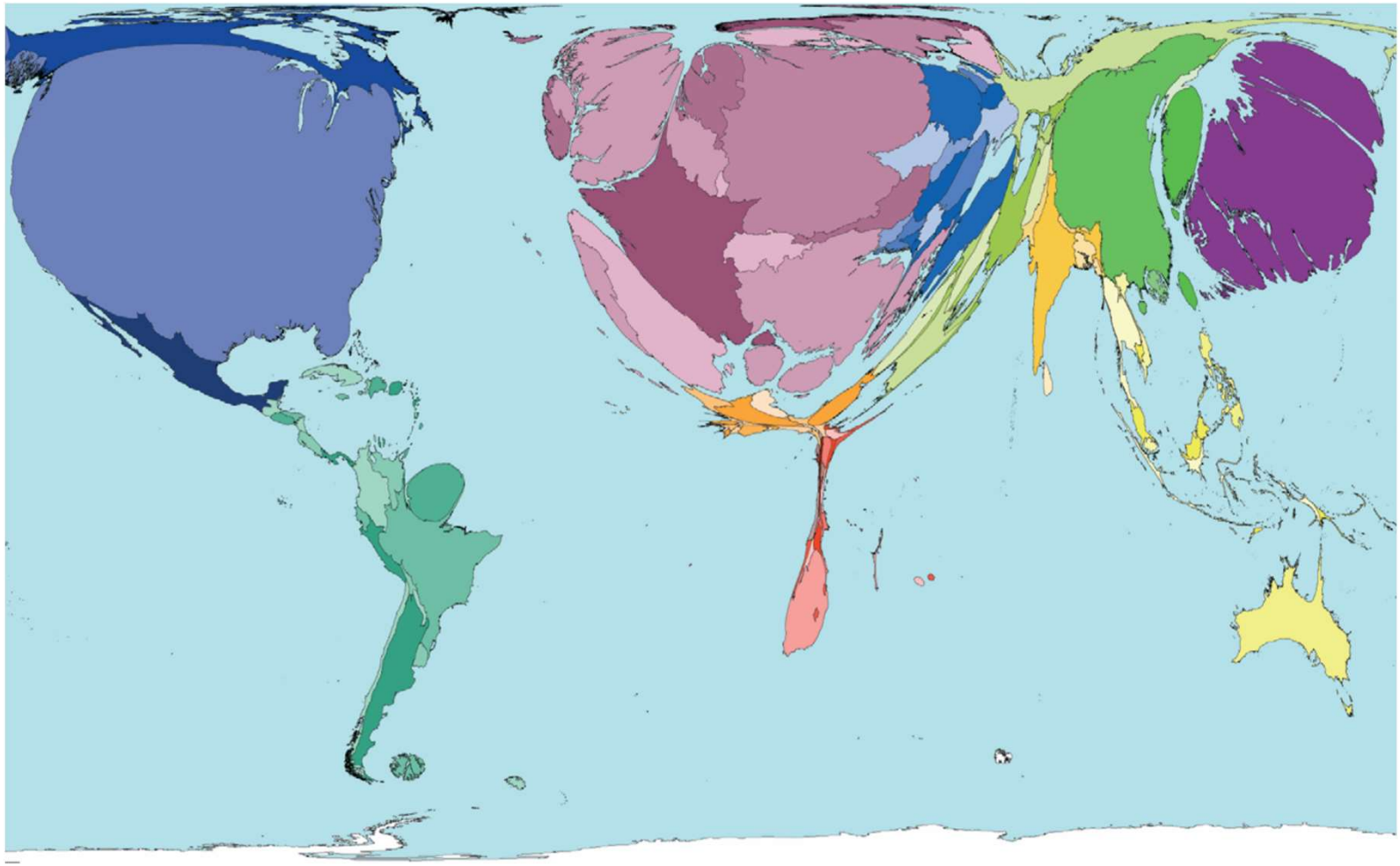
- Innovative and wearable devices provide prevention by monitoring patients and providing health data for remote, real-time analysis
- Patients identified to be at risk for certain disease will receive immediate prevention
- Prevention, however, in most cases, is not drug-based anymore
- Many will have chips implanted for identification, treatment or vaccination

…offering plenty of cannibalization risk but also plenty of opportunities to Gerresheimer

- Less blisters, tubes, containers - only one product, one dose
- Less packaging in total required
- Automated injectors have replaced traditional pills and injectables
- Implantable depots are in all of us
- Drug-coated devices (stents, tissue engineering, etc.) serve many patients
- One-time vaccinations has many treatments obsolete
- Artificial organs do not require traditional administration routes

10% of the world population eat up 90% of resources - plenty of room to grow

Global healthcare spending

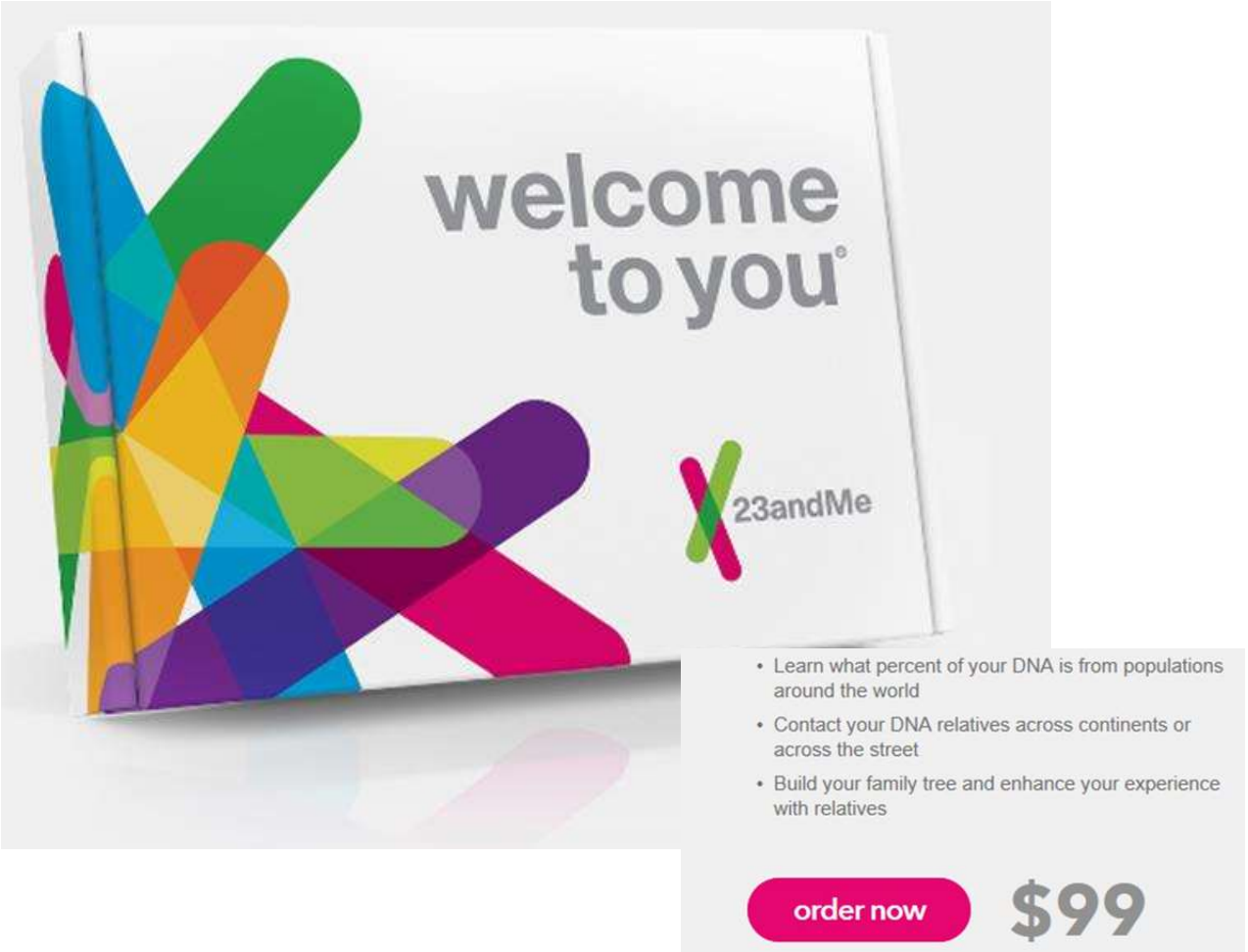


Source: worldmapper

Find out what your DNA says about you and your family

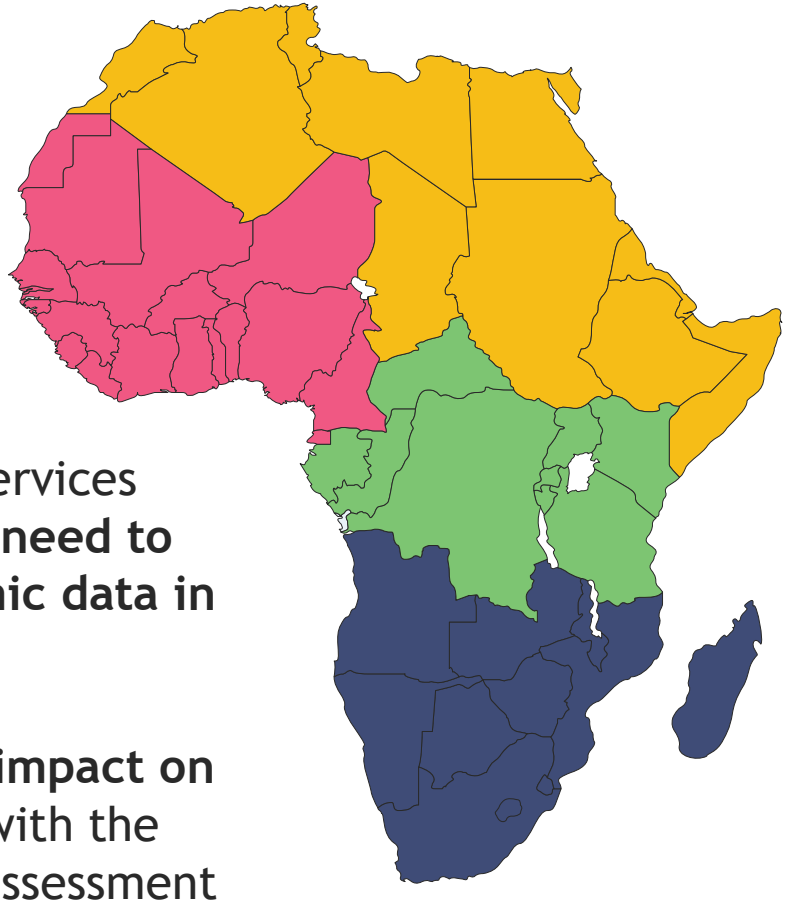
DNA sequencing as offered by 23andMe

- Patients can order DNA sequencing online, obtaining **full insight into their genome**
- With the help of physicians, consumers can read the **risk** of **developing** certain **diseases** from DNA and initiate steps to **prevent** them



Source: 23andMe

54gene targets at closing the “genomics knowledge gap” between the western and the 3rd world

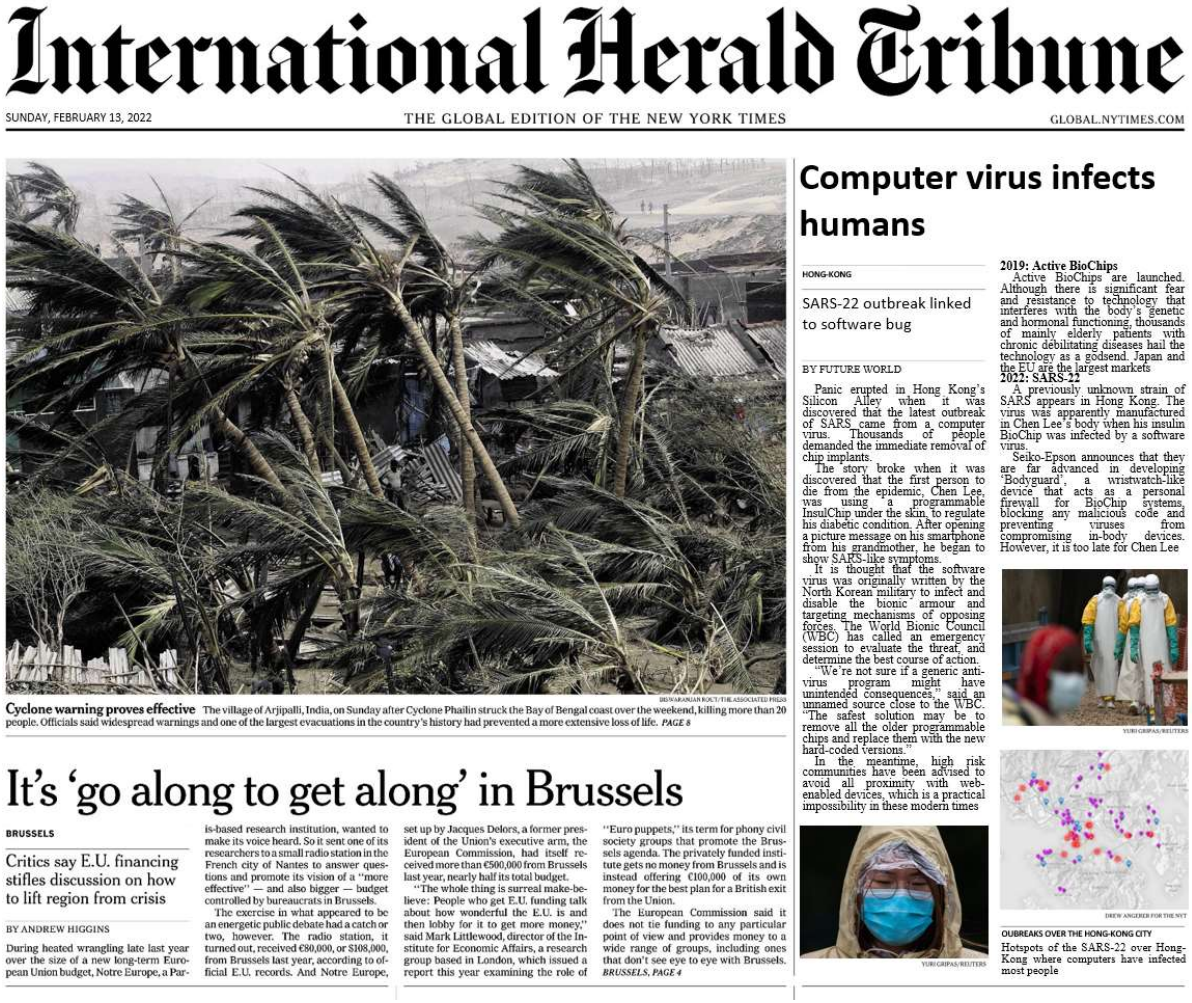


- **54 gene** is an African genomics research, services and development company **addressing the need to include under-represented African genomic data in research**

- **54 gene** strives to understand the **genetic impact on diseases penetrance and risk in Africans** with the goal to develop better diagnostic and risk assessment tests

Source: 54gene

In the future, GeneChips are a promising to cure chronic ailments such as diabetes but might along with massive security issues



International Herald Tribune

SUNDAY, FEBRUARY 13, 2022 — THE GLOBAL EDITION OF THE NEW YORK TIMES — GLOBAL.NYTIMES.COM

Cyclone warning proves effective The village of Arjipalli, India, on Sunday after Cyclone Phailin struck the Bay of Bengal coast over the weekend, killing more than 20 people. Officials said widespread warnings and one of the largest evacuations in the country's history had prevented a more extensive loss of life. *PAGE 8*

BISWARANJAN ROUT/THE ASSOCIATED PRESS

It's 'go along to get along' in Brussels

BRUSSELS

Critics say E.U. financing stifles discussion on how to lift region from crisis

BY ANDREW HIGGINS

During heated wrangling late last year over the size of a new long-term European Union budget, Notre Europe, a Paris-based research institution, wanted to make its voice heard. So it sent one of its researchers to a small radio station in the French city of Nantes to answer questions and promote its vision of a "more effective" — and also bigger — budget controlled by bureaucrats in Brussels.

The exercise in what appeared to be an energetic public debate had a catch or two, however. The radio station, it turned out, received €80,000, or $108,000, from Brussels last year, according to official E.U. records. And Notre Europe, set up by Jacques Delors, a former president of the Union's executive arm, the European Commission, had itself received more than €500,000 from Brussels last year, nearly half its total budget.

"The whole thing is surreal make-believe: People who get E.U. funding talk about how wonderful the E.U. is and then lobby for it to get more money," said Mark Littlewood, director of the Institute for Economic Affairs, a research group based in London, which issued a report this year examining the role of "Euro puppets," its term for phony civil society groups that promote the Brussels agenda. The privately funded institute gets no money from Brussels and is instead offering €100,000 of its own money for the best plan for a British exit from the Union.

The European Commission said it does not tie funding to any particular point of view and provides money to a wide range of groups, including ones that don't see eye to eye with Brussels. *BRUSSELS, PAGE 4*

Computer virus infects humans

HONG-KONG

SARS-22 outbreak linked to software bug

BY FUTURE WORLD

Panic erupted in Hong Kong's Silicon Alley when it was discovered that the latest outbreak of SARS came from a computer virus. Thousands of people demanded the immediate removal of chip implants.

The story broke when it was discovered that the first person to die from the epidemic, Chen Lee, was using a programmable InsulChip under the skin to regulate his diabetic condition. After opening a picture message on his smartphone from his grandmother, he began to show SARS-like symptoms.

It is thought that the software virus was originally written by the North Korean military to infect and disable the bionic armour and targeting mechanisms of opposing forces. The World Bionic Council (WBC) has called an emergency session to evaluate the threat, and determine the best course of action.

"We're not sure if a generic anti-virus program might have unintended consequences," said an unnamed source close to the WBC. "The safest solution may be to remove all the older programmable chips and replace them with the new hard-coded versions."

In the meantime, high risk communities have been advised to avoid all proximity with web-enabled devices, which is a practical impossibility in these modern times

2019: Active BioChips

Active BioChips are launched. Although there is significant fear and resistance to technology that interferes with the body's genetic and hormonal functioning, thousands of mainly elderly patients with chronic debilitating diseases hail the technology as a godsend. Japan and the EU are the largest markets

2022: SARS-22

A previously unknown strain of SARS appears in Hong Kong. The virus was apparently manufactured in Chen Lee's body when his insulin BioChip was infected by a software virus.

Seiko-Epson announces that they are far advanced in developing 'Bodyguard', a wristwatch-like device that acts as a personal firewall for BioChip systems, blocking any malicious code and preventing viruses from compromising in-body devices. However, it is too late for Chen Lee

YURI GRIPAS/REUTERS

DREW ANGERER FOR THE NYT

OUBREAKS OVER THE HONG-KONG CITY

Hotspots of the SARS-22 over Hong-Kong where computers have infected most people

Sunday, February 13th **2022**

"Computer virus infects humans - SARS-22 outbreak linked to software bug"

- Future scenario is likely to become reality, once **BioChips and DNA Microarrays** are implanted in humans on a mass scale
- Although these devices primarily take over passive functions, the **possibility exists to turn them active, thereby allowing them to write DNA encoding** to the living organism
- In order to achieve full therapeutic benefits, a wireless bi-directional communication is required

Source: Herald Tribune, stradoo