

impatient

PAUL SIMMS
JANUARY 2022

2022 Predictions





Good predictions are hard. They test your ability to understand today's moving forces. They require courage. And when you get them wrong, you look like an idiot.

But predicting is far more important than the prediction itself, and thinking about the future is essential. Most business plans are written with a concept of what's coming next, so working on that concept is time well invested. Our perception of what's possible has a dramatic impact on what transpires.

In 2022, most of us are hopeful for a better year after an extremely challenging 2020/21. This is lazy thinking. If we want a better 2022, now is the time for us to seize it. Doing so requires digging in... and looking up.

The webinar

These predictions were presented in a webinar on January 6, 2022, with co-host Jessica DaMassa.

To view the session or share with others, go to www.impatient.health/predictions

Impatient for 1 year

Impatient Health recently celebrated its first anniversary. As a company we now have 30 clients, all of whom can be described as pioneers. We work with those looking to be more ambitious and creative in finding and ensuring patient value.

If you want to challenge the status quo, brainstorm ideas or just workshop a few options, get in touch directly with Paul on paul@impatient.health

Learn more at www.impatient.health

(And if you just want a new CRM system, please go talk to someone else).

“I think it’s terribly dangerous for an artist to fulfil other people’s expectations. They generally produce their worst work when they do that. Always go a little further into the water than you feel you’re capable of, and go a little bit out of your depth.”

– David Bowie

2021 Predictions Review

How well did Paul do last year?
Let's find out.

1

A pharma company buys the consumer.

This was the idea that big pharma is increasingly focussed on 'becoming Ferrari' – ie. developing only specialty products, highly priced, designed for a small segment of the population. But the pandemic would expose the neglected middle, the chronic disease areas that required more attention and could be delivered by those outside R&D. And whilst there is a significant increase in investment into various beyond-the-pill efforts and various digital health activities in these diseases, my prediction went one step further and said that a pharma company would acquire a consumer-facing company in order to have that direct consumer relationship at a stroke. That hasn't happened. And it hasn't come any closer to reality.

Score: 0-1



2



A new era of unconscious wellness.

This was the observation that we are moving towards subscription models in more and more of what we do, and those subscription models often rely on algorithmic decision making. Obvious examples include Netflix which prioritises what you should watch and how it's described based on your previous viewing history. Other companies like Adobe and Apple have transformed themselves significantly through subscription services, and Amazon Prime is the biggest subscription of all time. When it comes to healthcare, these subscriptions would help consumers get better at managing their health through nudges and other behavioural interventions. Perhaps my prediction was a little too ambitious because although we can see the green shoots of this, it hasn't yet occurred in any meaningful way.

Score: 0-2

3



Vaccine nationalism exposes pharma's ugly side.

This prediction was made back in December 2020 when the first vaccines had just been approved. At that moment, the world was excited and grateful to the pharmaceutical industry for being able to achieve efficacy rates and production nobody thought was possible in such a short timespan. And whilst there is still an enormous amount of goodwill towards pharma, there is a lot of finger pointing. Everyone in Europe will recall AstraZeneca spent the first half of the year being shot down by politicians across the continent, prioritising certain jurisdictions such as the UK in the provision of vaccines and not communicating efficacy rates in the most senior, vulnerable patients as clearly as J&J paused its Europe rollout completely. As the year wore on, vaccine hesitancy rather than vaccine availability became the core issue, and governments became the primary target as omicron emerged. But just in the past couple of weeks, Albert Bourla of Pfizer was crowned CEO of the year by CNN whilst at the same time being exposed by the FT of being highly manipulative and despotic.

Companies will need to make serious progress in 'multivalent' vaccines that cover several variants and possibly even several virus types (including flu), and be far better at distributing outside western countries. Freeze-drying technology and new administration types (skin patches, inhalation, pressure injection) will be needed for hard-to-reach patients.

Score: 1-2

“Albert Bourla was our choice for all that Pfizer has done in a year where Covid vaccines went mainstream and helped stabilize America’s economy – and the world’s for that matter.” – CNN

“Pfizer never considered selling its Covid-19 shot without making a profit. It took an uncompromising stance, demanding \$100 a dose – \$200 a course, trying to play hardball during a time of national emergency. How could we possibly have a soft spot in our hearts for Pfizer?” – FT

“I’m satisfied that the company is doing financially very well, but even more satisfied when I go into a restaurant and get a standing ovation because everybody feels that we saved the world.” – Albert Bourla

“He hasn’t saved the world. He could have done it but he hasn’t. Vaccine apartheid and restricted production continue to fuel the spread of the coronavirus.” – Winnie Byanyima, Executive Director, United Nations AIDS Program

“[Pfizer’s conditions were] abusive, during a time when due to the emergency governments have no space to say no.” – Jarbas Barbosa, Pan-American Health Organization

4

Pharma leaps to a web 2.0 model.

I talked last year about how the pandemic shouldn't just be an accelerant, but that it should allow new business models to appear. The analogy of Web 1.0 (the original internet firms like Altavista, Geocities, AOL and Lycos, which have since disappeared) and web 2.0 (companies we're all familiar with, which now dominate) is a useful one, because it illustrates that when we reached a digitisation threshold in the world – ie. enough people having access to fast internet – different business models became possible that replaced the old ones in dramatic fashion. So far, a few models are emerging, for example the at-risk commercialisation model being pursued by Eversana, but others are still emergent and yet to gain real traction.

Score: 2-2



Digital health kills telehealth.

My prediction was that the telehealth would be here to stay, but as a basic technology it would quickly be found to be inferior. Telehealth spiked during 2020, but fell to lower, more stable levels in 2021 (13-17% of all visits), and telehealth companies are actually really struggling with profitability. Yet, unsurprisingly, consumer and provider attitudes are forever changed, heralding what is the most interesting change – a change in the nature of care. People now realise that digitisation doesn't just provide access via technology, but a reimagining of what healthcare actually is. Providers are now reorganizing practices and processes around new ways of interacting, some of which does not involve one-to-one interaction but new solutions and devices for the home. Meanwhile, digital health startup investment has grown again record levels: by halfway through 2021 more money had been raised than in the whole of 2020, around \$15bn.

“Telehealth has a much bigger role to play than just carrying out transactions. What was once all about ‘access to care’ is now about ‘quality of care’. This is a major turning point – a meaningful relationship to care through technology.” – Roy Schoenberg, President & CEO, Amwell, interviewed by Jessica DaMassa, Feb 2021

Score: 2-2

5





Amazon wins healthcare – as a side gig.

Does Amazon make any money from its Prime Video service? Actually, no. But it does ensure that more Amazon Prime subscriptions are sustained as a result. And sustaining those subscriptions is the key to the company's future. Amazon has incredible access to cheap capital, can create healthcare services at a loss if it wants to, but despite that, many people think Amazon withdrew from healthcare when it announced the cancellation of its Haven initiative with JP Morgan and Berkshire Hathaway at the end of 2020. This is not the case, yet Amazon has failed to make any further major healthcare announcements in 2021 beyond the expansion of AmazonCare. We have not yet seen a 'Prime Health' offering yet, and Amazon has form when it comes to making public the services it develops internally, but with the recent CEO transition I don't believe this is over yet. Let's watch this space.

Score: 2-2



Pharma removes its mask for the first time.

In late 2020 and early 2021 the initial take-up of Covid vaccines was strong; I attributed this to an enlightened communications strategy from the companies that developed the first vaccines, and that such success would create a new transparency, authenticity and relatability amongst pharma firms. In the end, they learned nothing and went back to their old ways.

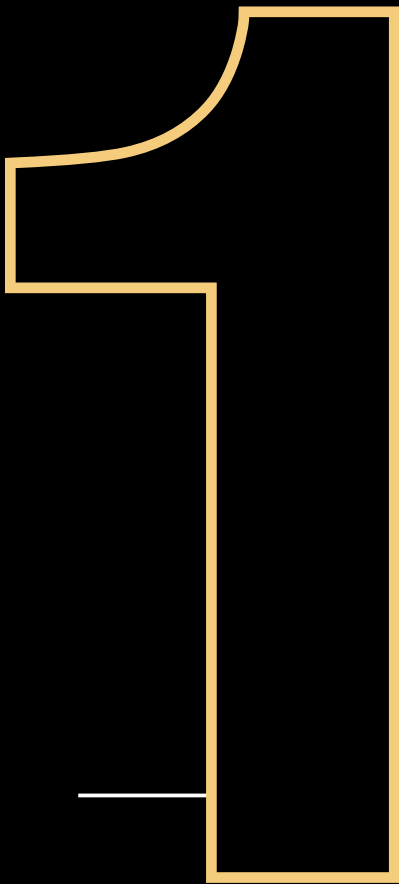
Score: 2-3

FINAL SCORE

2 – 3

Paul loses.
(And that's OK!)





PHARMA
GOES
DIGITAL
NATIVE

And Gen Z kills primary care

What was the most popular online property in 2021? Most people would suggest Google, Facebook or YouTube perhaps.

The truth is that Google was removed from its perch for the first time in many years during 2021 by a relatively new player:

2020

1. Google
2. Facebook
3. Microsoft
4. Apple
5. Netflix
6. Amazon
- 7. TikTok**
8. YouTube
9. Instagram
10. Twitter

2021

- 1. TikTok**
2. Google
3. Facebook
4. Microsoft
5. Apple
6. Amazon
7. Netflix
8. YouTube
9. Twitter
10. WhatsApp

The rise of TikTok from 7th to 1st in just a year is impressive, and primarily due to the emerging generation, Gen Z, made up of people born between 1997 and 2012 (between 9 and 24 years old today), maturing fast. Of this generation:

- 63% use TikTok (up from 50% in 2020)
- 57% use Instagram (down from 63% in 2020)
- 54% use Snapchat (holding steady)
- Twitch & Discord rising fast

This is a generation now entering the professional world, and changing the rules as they do so.

Anyone who watched the new Netflix comedy 'Don't Look Up' over the holiday period is probably despairing over the state of a world which prioritises celebrity stories and conspiracy theories over actual news, even when the news brings the end of the world.

But as a new generation becomes professional it also becomes the consumer and provider of healthcare. Already the way we think about the provision of health. We already mentioned the evolution beyond basic telehealth into a digital reimagining of what healthcare is. We now have a group of people who don't remember a world without smartphones, and the touchscreen or voice is the most natural interface. They don't understand why anyone would rely on an email account or store their life record in anything other than social media.

Here are some attributes we need to get to grips with:

- **They're digital (health) natives** – this is a generation that would far prefer to receive healthcare online, often has no local GP and in many cases doesn't want one. They also can't see why online communication is inferior for most conversations.
- **This is the least brand-loyal of all generations** – accustomed to leave with a click, and brands come and go (or get cancelled) so fast that allegiance is a fleeting concept. Brands need to prove themselves - not just say they're great - before trust is generated.
- **Being young, they are naturally price-sensitive** and will often go to great lengths to get a bargain. But they also see it natural to spend the money they have on digital objects/coins, considered no more 'wasteful' than previous generations were when purchasing a brand-name item.
- **They are naturally cynical** and instantly reject any corporate-speak or glossy story. Adventure, entertainment and shareability are far more appealing than quality.
- **That said, authenticity, transparency and legitimacy are highly prized**, again beyond quality and relevance. Far better to be vulnerable, truthful, credible and inferior than filtered, polished and unrealistic.
- **They do not see any need for an offline component** to a product or service. Think DVNB (Digital Vertical Native Brand) as the way forward.
- **Storage and documentation are old-fashioned constructs.** There is an endless supply of content, so why keep hold of anything? And no need to decide what to do when the algorithm can passively prioritise what comes next.
- **Game dynamics are fundamental to every form of service.** Even influencers are no longer brands or celebrities; they're virtual characters or avatars with high achievements and ratings. Ads are much more than brand promotions, they are reciprocal rewards for originators/influencers who provide content.
- **The metaverse is already home.** Only those inside this world are relevant. (Facebook's version of the Metaverse is already dead on arrival – Roblox, Fortnite and others already provide the community and game world, whilst companies like Apple are better placed to capitalise.)

Even companies you might consider digitally-savvy, such as Spotify, admit that they are unable to appeal to the Gen Z generation that eschews conventional format types.

Millennial movements and the death of traditional primary care

The emergence of Gen Z isn't the only shift taking place. Amongst others, especially millennials, there is further change, in particular a desire to make work and home life a far more fluid construct.

99% of the people who have contracted, endured and developed antibodies for Covid-19 have not needed a hospital, much less a doctor's office. Remote healthcare has become not just normalised but expected.

Airbnb suffered an instant 80% drop in revenues when the pandemic lockdowns hit. The CEO was immediately forced to make significant organisational change, becoming more of a lifestyle rather than travel-focussed firm. He now notes that 20% of his bookings - and by far the fastest growing segment - are from those booking stays for a month or longer - people choosing to live rather than simply visit, or to use it as a local workplace. They also see a huge rise in bookings starting on Mondays, requesting internet speed checks, and requiring workspaces.

There is a clear trend towards more flexible living, and we are far more likely to choose providers and services that allow us to share data from remote monitoring devices. It's analogous to banking: a typical bank branch requires around \$50m in deposits/loans to be sustainable, and the alternative convenience of online banking has meant that far fewer meet this threshold: 30,000 branches have closed over the past decade in the US alone.

But don't confuse branches closing with less access. There are 1.7bn people in the world who have no bank account and far more of them can benefit from an online service. The same will be true of healthcare, with digital service reaching far more than traditional ever could. This is the beginning of the end for the GP's office, and it's no bad thing.

2

AMAZON

BUYS

TEVA

Amazon, currently valued at \$1.75 trillion, has a habit of acquiring single companies in a new industry. There are several reasons why it does this.



Vertical integration is part of Amazon's fundamental 'customer obsession' philosophy, reducing barriers to a smooth and useful experience. This doesn't mean it needs to buy customer-facing businesses, but it does buy things that ultimately aid a better flow. A good example of this is the recent purchase of MGM Studios in order to facilitate the production of content for its original Prime Video content. The acquisition of Whole Foods in 2017 bought a local distribution network and a foray into high-end food retailing, both of which have been built upon since purchase.

By acquiring just one company in an industry, it never becomes too dominant in one space – other competitors are still intact - and is able to avoid monopoly law, essential in an age of growing negative sentiment towards big tech.

Amazon is heavily invested in healthcare already, with Pillpack and AmazonCare its major initiatives to date, with the major Haven venture with JP Morgan and Berkshire Hathaway discontinued yet not abandoned in late 2020. Also 2021 saw the launch of AmazonDx (focussed on Covid-19 for now) and a number of smaller initiatives designed to 'complete the circle.'

Amazon's challenge is now to maintain the trajectory of their stock price, needing to increase their top line revenues by almost \$250 billion in the next 2 years. Amazon doesn't necessarily want to go into healthcare, but it has to.

However, Amazon does not demonstrate any desire to become a direct healthcare provider or insurer despite these being customer-facing, which would change its business model and add new risks to the business.

Google's DeepMind division recently launched Isomorphic Labs, a new initiative to discover drugs using AI (building on their major leap in protein folding science), however the nature of Amazon's business is that it would far rather be involved in a venture where value is created by being operationally, rather than scientifically, excellent.

Looking at the landscape of available companies for purchase, Sandoz is likely to be unloaded by Novartis during 2022, but TEVA is more likely as (a) the largest generics company with the widest portfolio in the US and Europe, (b) good value given that it has fallen from an elevated former price, still carrying \$26bn debt and with a low (non-investment grade) credit rating, and falling revenues from \$22bn in 2017 to \$16bn today, (c) it has been making itself operationally better over the past few years so far leaner than it was previously, (d) a market value within Amazon's buying range, costing less than 10% annual revenues.

An Amazon-owned generics firm would integrate directly with Pillpack and would be able to cover most conditions. It would potentially allow the creation of a new B2B retail and distribution arm (something that others could join or emulate) and, in owning supply, would provide the leverage to create a new, more efficient relationship between insurers, providers and employers/government.

If medicines are bought and sold on a B2B ecommerce platform, driven by Amazon-like technology, how would it change pharma's commercial model?

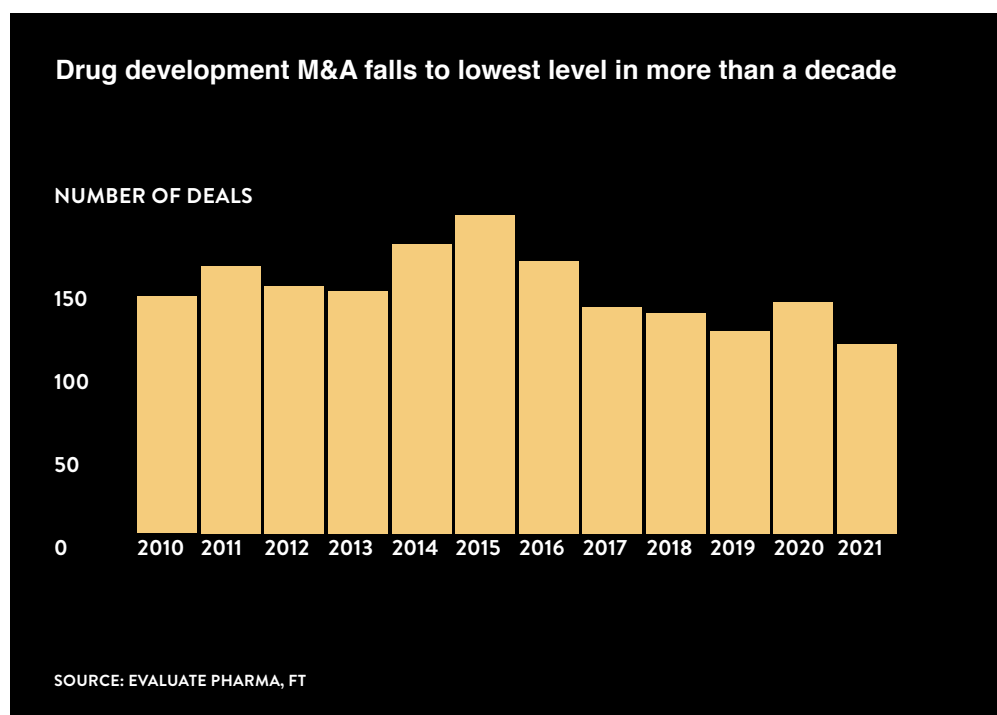
BIOTECH

BURSTS

3

Biotech is living on borrowed time. 2021 broke records for the amount of capital raised, and there is plenty of money still floating around from both venture capital and big pharma looking to boost pipelines.

Yet there was a 'slow crash' of biotech stocks in the second half of 2021. Somehow, many in big pharma didn't appear to really notice. And now companies are being pushed even lower over threats of increased regulation and bureaucracy fears. 2021 ended up as a damp squib:



Given that larger companies now rely so heavily on external innovation to create their pipelines (a key reason why so much funding has been provided in the first place), understanding the dynamics of biotech cashflow has become essential for aspiring pharma managers.

Biotech's bubble grew swift and fast in 2021. The median time from founding to IPO has gone from 10 years in 2013 to only 4 years in 2021. In the past seven

quarters, more than 80% of IPOs were preclinical or Phase 1, nearly the inverse of a decade ago. These are young startups with mostly preclinical or biomarker (vs clinical endpoint) datasets. With so much money, more than 120 biotechs will each burn through more than \$100m this year (up from around 20 in 2016).

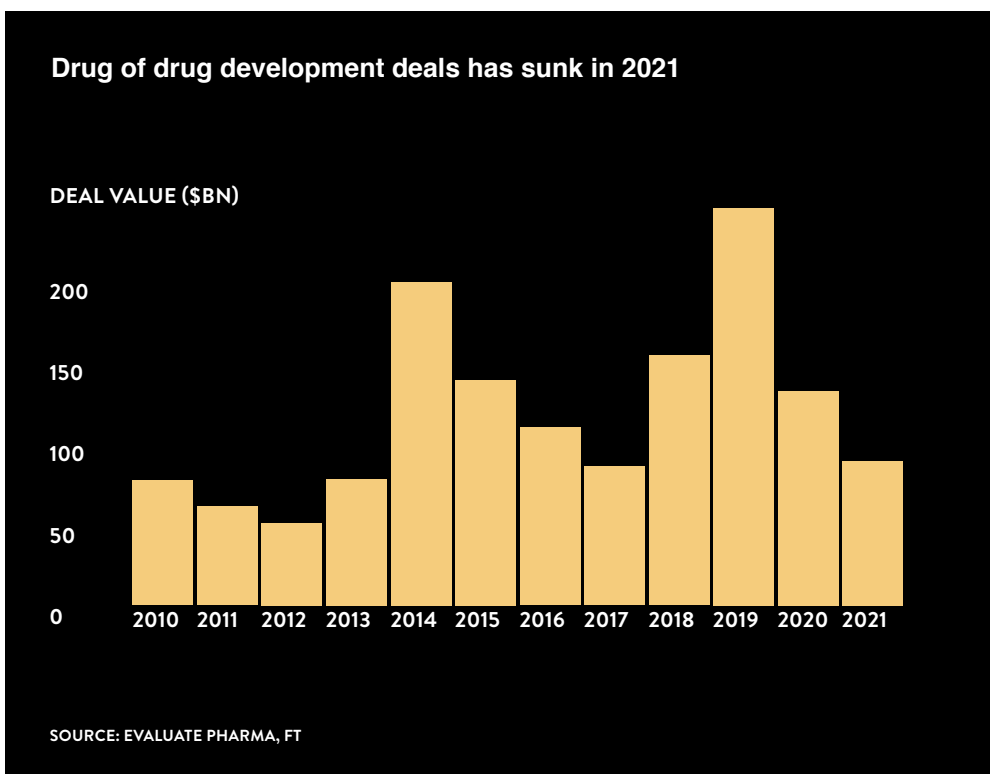
Some of the big names initially posted incredible rises. Between November 2020 and February 2021, Beam Therapeutics shares went from \$36 to \$115. CRISPR Therapeutics went from \$90 to \$200; Fate Therapeutics: \$48 to \$116; Editas Medicine: \$30 to \$90.

And then came the long fall. Today, Beam trades for \$82; CRISPR \$79; Editas back down to \$27; and Fate \$59. The XBI is down 19%, the sector's worst performance since at least 2008. It's even bleaker when viewed against the S&P 500's 23% rise.

Yet, here in 2022, there is still money flowing in, and the appetite for new IPOs has not abated (partly fuelled by our industry's heavy use of SPACs, which cut down heavily on bureaucracy but typically require a merger within 2 years, encouraging panic-buying). There were 149 biotech IPOs in 2020-21 compared to just 83 in 2018-19, and analysts expect that rate to continue through Q1 2022.

Where is it all going? The market is unsustainable. By the end of 2022 I predict that the double-digit dips already seen in the final months of 2021 will precipitate a larger fall and that overall, sentiment will be concretely lower.

If biotech collapses and the funding goes with it, what will the implications be for larger pharma companies? What does 'desperate measures' look like in portfolio planning if there are less biotech innovators to choose from?



“We’ve seen an absolutely bonkers and out-of-control flood of initial public offerings. Too many of these new issuers were preclinical, poor quality, or both — overwhelming the market and robbing capital and attention from more deserving biotech companies. I’m old enough to remember when it was the norm for these ultra-risky ventures to remain private until they could produce credible data in patients. No longer! Today, the risk is routinely dumped onto the public markets, sold to investors with a wink and an interesting story.”

ADAM FEUERSTEIN
STAT NEWS ON DEC 21, 2021

“I don’t see any reason why the U.S. funding for biotechs next year is going to slow down.”

JOSHUA CHAO
SENIOR ANALYST
PITCHBOOK ON DEC 29, 2021

PHARMA'S

REPUTATION

HITS WHERE

IT HURTS

4

I spoke earlier about the impact of Gen Z as consumers and HCPs, however this is a group also now having an impact on investment and trading.

'Meme stocks' became one of the buzz-phrases of 2021 on the back of an incredible, legal, collective share price manipulation by a group of investors that wanted to punish hedge funds for ruthlessly shorting certain companies. They were able to raise the price completely independently of fundamentals. And it hasn't stopped. So far, most meme-trading activity has been more akin to playing a game, catching out unsuspecting players that didn't know they were part of it until it was too late. But this will become a far more sophisticated and coordinated endeavour in the near future. Regulators are struggling to keep it in check - these events are neither an example of 'pump and dump', in which the shares of a firm are boosted then sold quickly, nor a cybersmear scheme in which a short-seller publishes malicious rumours about a company. Instead, it's 'pump, hold and turn the screw', an action that sits a long way outside existing frameworks of market behaviour.

Google's top 10 global news searches of 2021:

1. Afghanistan
2. **AMC stock**
3. Covid vaccine
4. **Dogecoin**
5. **GME stock**
6. Stimulus check
7. Georgia Senate race
8. Hurricane Ida
9. COVID
10. **Ethereum price**

Meme-trading doesn't have to be negative, however. Given that the share price of Tesla correlates almost perfectly with popular game-trading app Robinhood and Elon Musk's propensity to stoke the conversation, and the fact the company valuation has no longer any real relation to earnings, the electric car company has benefitted from a generation of traders who are undeniably militant in their support, propping up continued price rises.

Whether positive or negative, now that this new-found manipulation superpower has been discovered, it is being institutionalised and codified. Companies will find that their reputation and authenticity will directly impact their worth, irrespective of their commercial performance, ushering in a new age of corporate sustainability that looks very different from what we've seen before. Pharma companies, as illustrated many times before, have presided over multiple scandals – but have survived as profits have rarely been affected significantly. The rules are different now.

If reputation trading goes mainstream, how will pharma act to avoid negatives and secure positives?

THE

BEGINNING OF

THE END FOR

PHARMA'S

COMMERCIAL

TEAMS

5

Once upon a time, hotels relied on travel agents. They then discovered the internet, and built websites to reach customers directly.

This period was short-lived, because very quickly consumers realised they didn't have time to visit every hotel's website individually, no matter how convenient for the hotel. Instead, they gravitated towards a new generation of portals, which eventually grew into the most valuable and popular destinations – names like Tripadvisor, booking.com and Expedia became the natural go-to places for starting a new trip. Nowadays, a hotel's budget is far better directed towards optimising and managing their presences on such portals.

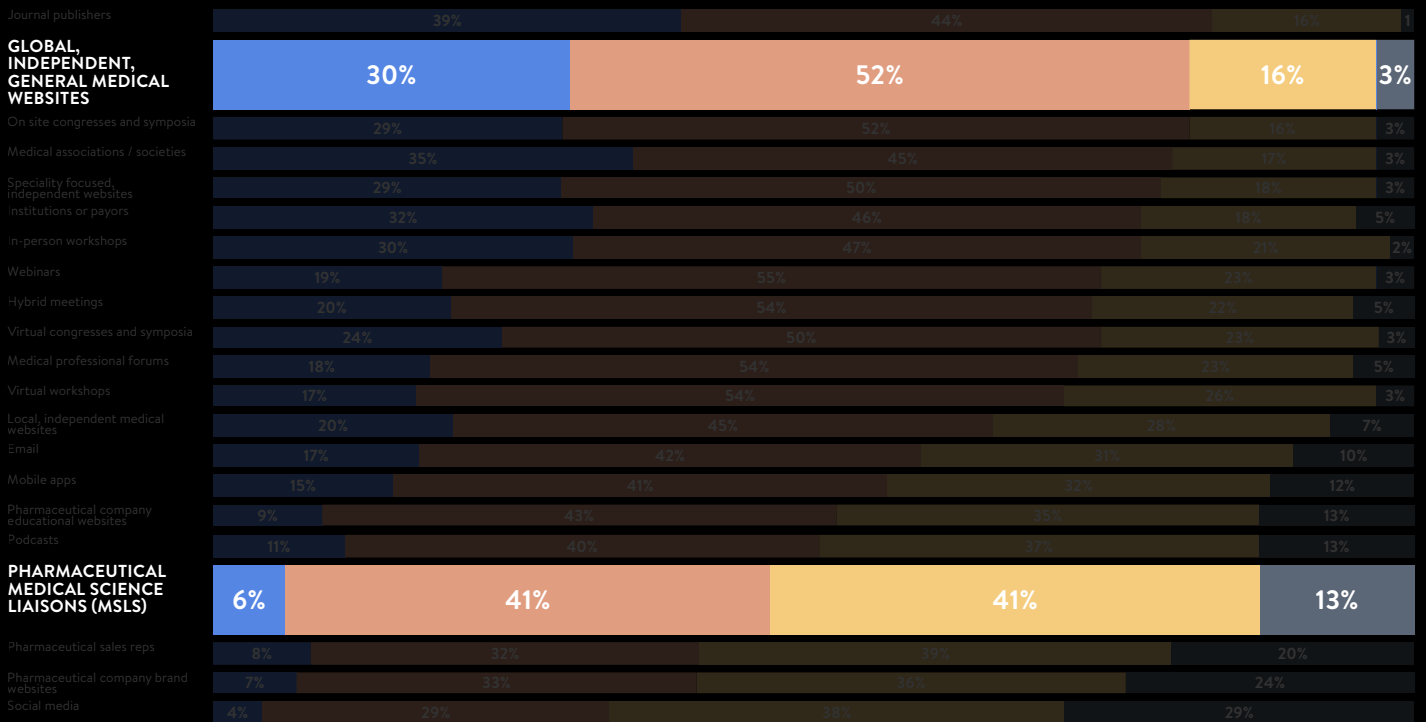
Meanwhile, commercial pharma teams have responded to the pandemic by creating branded content sites; each themed for a single company and single therapy, in an attempt to control the conversation and affix the company logo to every interaction. In many ways it's like going back to the late-90s internet.

Customers will vote with their mice, and click away from places that don't provide value. Increasingly they will gravitate towards a small number of central locations where good UX, good knowledge and trusted interaction with peers will generate a 'safe space' for learning and sharing.

Pharma's short-sighted approaches will hasten the demise of commercial teams, which invest in providing valuable information yet shoot themselves in the foot at the same time. Unfortunately the latest research from EPG Health shows the trend will continue into 2022, with funds directed towards brand awareness rather than independent portals:

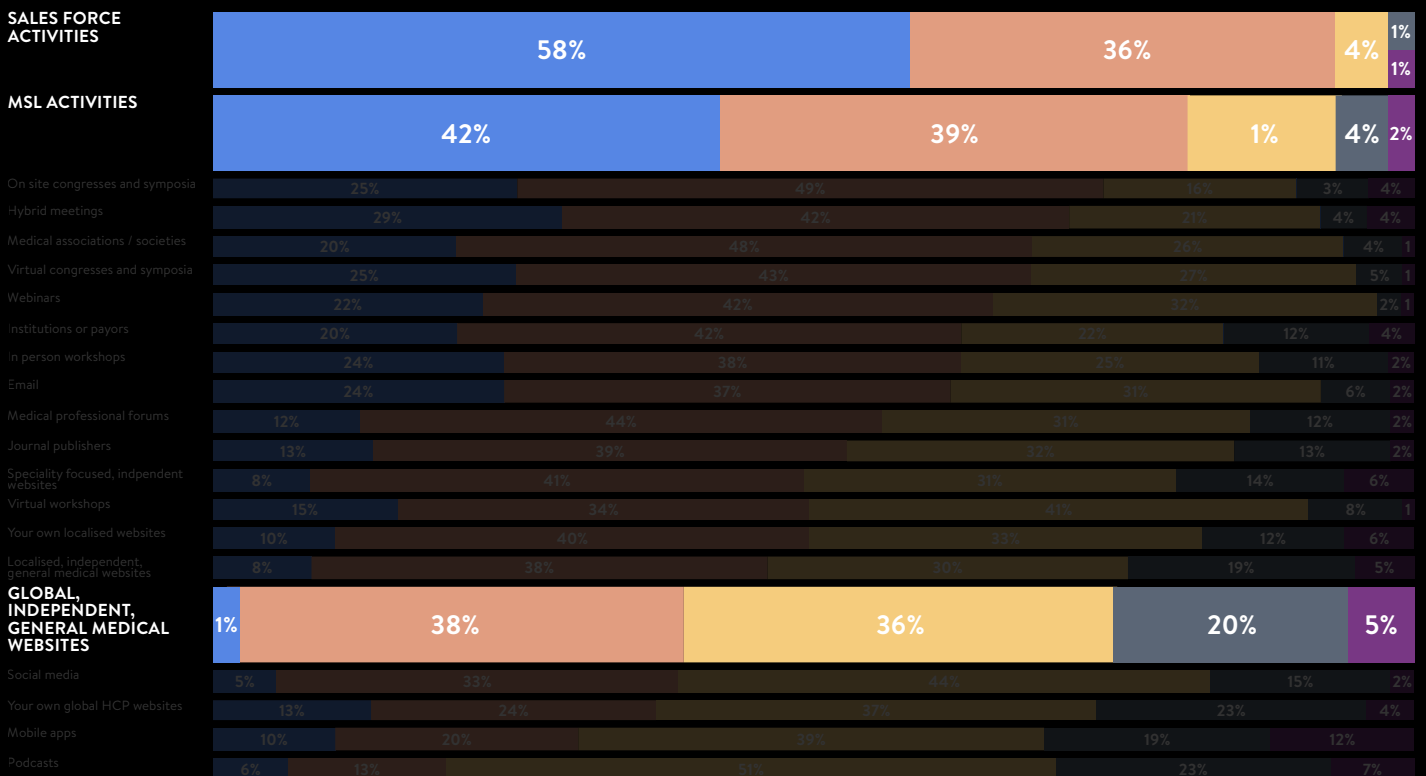
HCP:

How important to you are the following sources of scientific information?



PHARMA:

How important are the following channels for delivering scientific information to HCPs?



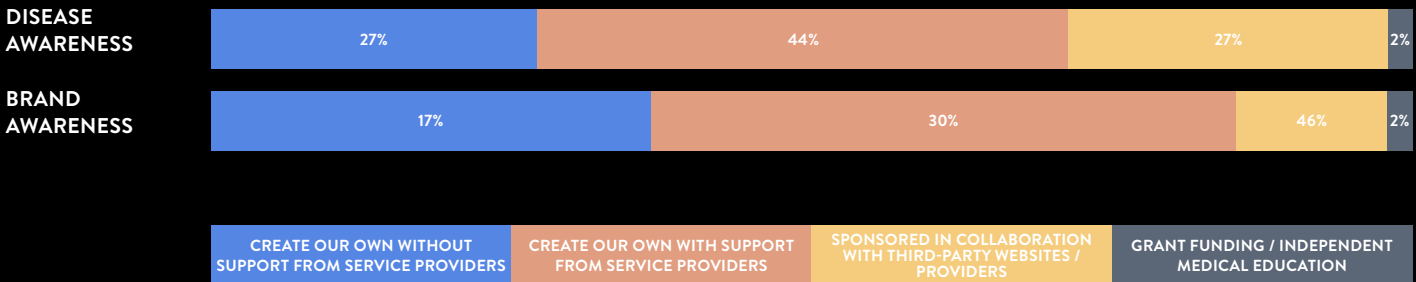
PHARMA:

How do you anticipate pharma budgets will be allocated next year?



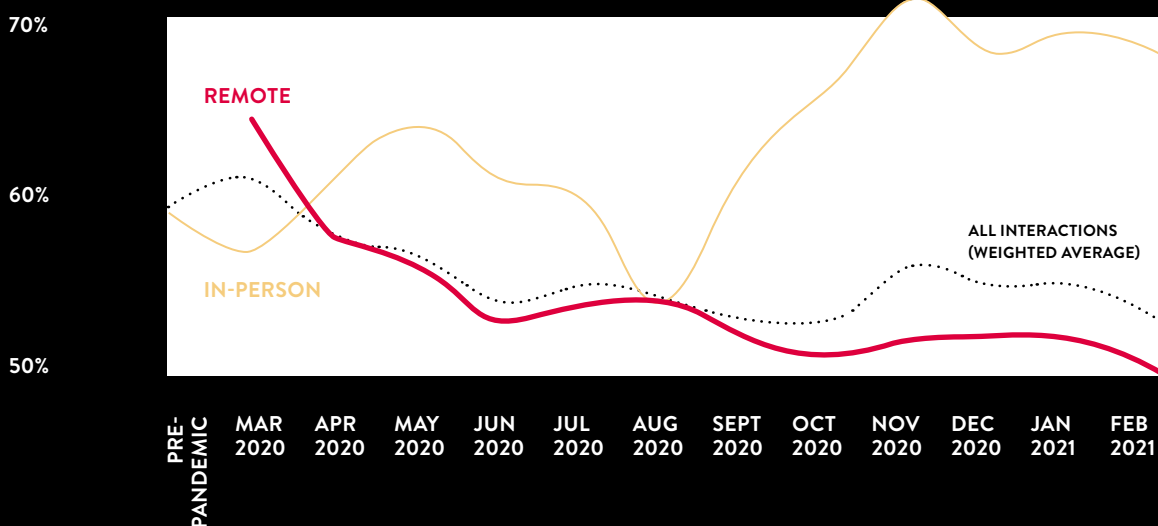
PHARMA:

What funding model dominates supply?



This is compounded by recent research demonstrating that the effectiveness of sales reps, when engaged in digital calls, has fallen sharply during the pandemic. ZoomRx measured as physician likelihood to prescribe after a sales rep encounter as dipping below 50% in 2021, lower than the pre-pandemic level.

Impact on prescribing – rolling 3-month average



“We don’t see any signs of rebound or recovery (in digital visit impact) over time. There was a dramatic decline in impact from March to June last year and then pretty much a steady state over the past eight months.”

TY HARKNESS

ZOOMRX

Some enlightened managers, however, are breaking away. In the UK, the NHS is trying to develop an entirely new procurement and payment approach with the pharmaceutical industry, having now piloted it in select treatment areas. This is much more than the value-based pricing models that have been debated endlessly over the past decade.

The idea of the payment approach is to move away from paying for individual medicines on a pack-by-pack basis and, instead, make an annual payment based on the health benefits to patients and the value to the NHS.

So far, the pilots are demonstrating that this payment model can be a win-win for health systems and industry – NHS patients will be able to benefit from a secure supply of new medicines, while pharmaceutical companies will be able to reliably forecast, plan and manage their return on investment.

This has allowed greater funds (and thus greater R&D) into underdeveloped areas including antimicrobials, working with companies like Shionogi and Pfizer. It is believed that this will ultimately drive down prices to generate savings for the NHS to ensure that they have more efficient access and reduce inequalities.

The managing director of one company informed me that he believes we'll see sales reps disappearing very quickly. Our role, as an industry, will not be to actually sell drugs, but rather to work in partnership with the healthcare system by driving technology collaborations and fundamentally align our objectives with those of providers like the NHS to improve patient outcomes, reduce unwanted events and ensure a more sustainable healthcare system.

Perhaps a single-payer system like the UK makes this feasible. However other countries are watching and implementing their own similar pilot arrangements. Consolidated procurement of branded medicines will change the nature of commercial pharma, and pharma companies will rely far more on their national partnering abilities than their local sweet-talking.

Companies will also invest more in developing endpoints together with providers. A recent example is AbbVie, Janssen, Novartis and UCB partnering with the Digital Medicine Society (DiMe) to develop a new digital endpoint for Atopic Dermatitis, where night-time scratching – measured using wearable sensors such as an accelerometers in a smartwatch – can help provide a more complete and meaningful picture of the impact on patients and incorporating this as a target measurement in product development. There has yet to be a new medicine approved on the basis of one of these endpoints, generally due to such fragmented efforts to date. Collaboration enables standardisation, credibility and the ability to create something that works for the provider who is often burdened with measurement.

6

NATIONALISM

AS THE PATH

TO HEALTH

EQUITY

In October 2021, Boris Johnson stood up to address his party at his annual party conference, saying:

“How have we managed to open up [our economy] ahead of so many of our friends? You know the answer, its because of the roll-out of that vaccine: a UK phenomenon, the magic potion invented in Oxford University and bottled in Wales, distributed at incredible speed to vaccination centres everywhere.

I saw the army in Glasgow firing staple guns like carbines as they set up a huge vaccination centre. And in Fermanagh I saw the needles go in like a collective sewing machine, and they vaccinated so rapidly, faster than any other major economy in the world. And just as we used our new freedoms to accelerate the vaccine rollout, we are going to use our Brexit freedoms to do things differently.”

BORIS JOHNSON

OCT 2021



Many Brits will say that Boris Johnson doesn't have long left in office, but what you see here is an example of what I call vaccine nationalism; a need to control - and boast about - a national supply chain, a regulatory process, a treatment provision, a destiny. This is great for stoking local support, but it of course amounts to the prevention of the global free movement of medicine in times of global crisis such as Covid-19.

And the trend, I'm afraid, will not be to open borders and share more, despite the heartening stories of vaccine donations by some progressive governments. It will be far more about hoarding and playing hardball. This was an approach instigated by companies like Pfizer, who would only provide vaccines to specific countries in return for sweeping changes including legal immunity from any ill effects as reported in December by the FT. At the time of writing, we are nearing 50% of the world fully vaccinated, but developing countries are at a mere 8.5%. To avoid being so powerless and dependent in the future, nations will set up their own regulatory systems and conditions, preferring not to 'outsource the health of their nation to a foreign body', echoing George W Bush's famous "we should never outsource America's national security line' when referring to the UN.

Ironically, countries will describe this as a way of ensuring health equity, of ensuring that the health needs of all the country's citizens can be fairly met. And although that doesn't meet the generally agreed definition, it will likely be the rules we have to play with for the foreseeable future.

What it will also do is create new markets for medicines beyond Covid. Currently, launching a new medicine is only ever done in one country - the United States. But a wider tapestry of local regulators and distributors would make it feasible to approach other countries first. I spoke with the CEO of one biotech company recently who told me that we are inadvertently building a new pharmaceutical landscape, and he's so excited that he doesn't have to depend solely on America anymore.

I predict that a more national approach to medicine distribution will lead to a redrawing of the access paradigm and thus the launch planning of new treatments, despite prices remaining highest in the US for the foreseeable.

What would your company do if access and distribution became easier in other countries?

**REIMAGINING
MEDICINE:**

A

PSYCHEDELIC

POWER

TRIP



‘Reimagining medicine’ is Novartis’ tagline. But ‘reimagining’ can become an adjective rather than a verb. Psychedelic medicines which allow our brains to respond in a more plastic way, reimagining and releasing trauma, describe the fastest growing new category.

My prediction is that this new category, alongside cannabis, makes the leap to big pharma portfolios for the first time.

Some still think of Woodstock when they hear about psychedelics, but drugs like ketamine - in clinically controlled conditions - are one of the safest out there. Indeed, ketamine has been identified by the World Health Organisation as an essential medicine: if your child was to break a bone and receive an anaesthetic, ketamine would typically be a first choice treatment over opioids and other options.

These drugs are also very effective. Long-stigmatized drugs like Esketamine (approved as the Spravato nasal spray in 2019), MDMA (actually invented by Merck scientists in 1912) and psilocybin (magic mushrooms, where the US government is now funding the first therapeutic research in 50 years) are advancing rapidly through clinical trials for treatments of a range of mental health conditions in a world where one in four people suffer from these disorders.

Over the past 18 months, while most of us have been distracted by the pandemic, the psychedelic industry has exploded. Companies that had for years quietly pursued research went public. Dozens of startups launched. And VCs began to pay serious attention. An industry that a year ago had a market cap of less than \$1bn suddenly houses four companies that each individually have a greater-than-billion-dollar valuation.

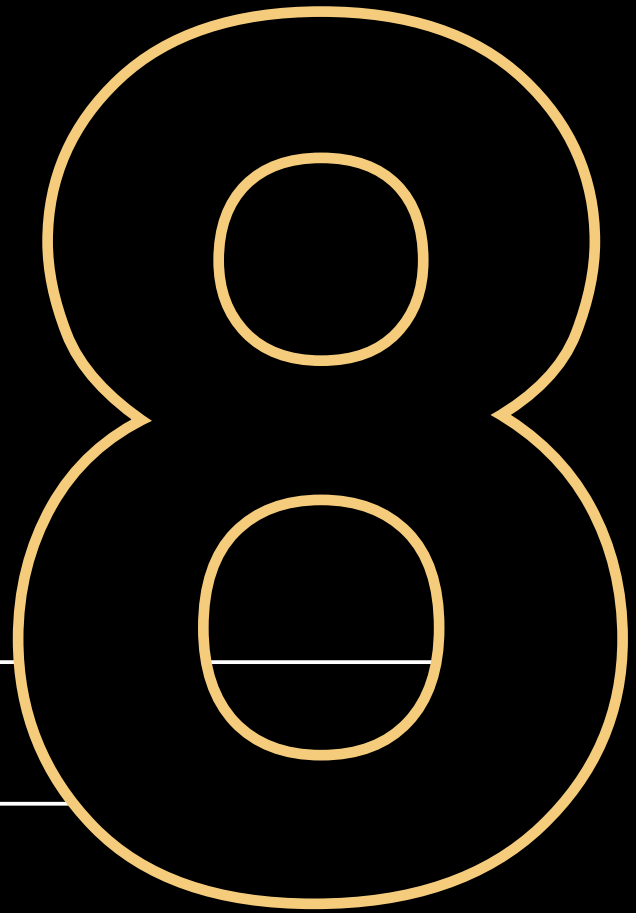
Far from being central to counterculture as they were in the 50s and 60s, psychedelics have really blossomed partly due to serious efforts from Johns Hopkins, NYU and Imperial College which have constructed state-of-the-art research facilities. Psychedelics are now coming online with FDA-approved ketamine-assisted therapy, and we expect MDMA- and psilocybin-assisted therapy to be approved by the FDA and Health Canada during the next 18 months to four years. Developers are trying to distance themselves from a separate movement, to legalize recreational use of these drugs, and instead take the very sober path to regulatory approval. Indeed the CEO of the largest psychedelics company, Atai, believes this approach could create a backlash.

But there are some hurdles. As we know, the nature of modern, allopathic medicine is that we need to identify the ‘wrong’ that needs to be righted and cured, and our regulatory system is designed to accommodate that approach. However, there is a great deal of potential to use psychedelic assisted therapy from an integrated, functional or preventative approach, optimising and enhancing what’s right. Most doctors and practitioners say that once psychedelics get approved they’ll be used off-label, but to be approved in the first place they need the traditional outcome measurements to be proven in the normal way, and insurance companies will need to be able to gauge value. That value is looking promising: for example; MAPS has achieved breakthrough FDA designation and is conducting a second Phase III trial with MDMA-assisted therapies, so far demonstrating an effective 67% cure rate; remarkable when you consider that current PTSD treatment options seek a 30% improvement in symptoms.

The numbers can’t be ignored. Pharma companies looking for clinical benefit will see the rapid professionalizing of the cannabis industry and seize the opportunity to add psychedelics to their pipelines.



**ELON
MUSK
GETS
INTO
PHARMA**



If Elon Musk did set his sights on pharma, it would certainly be an interesting day. A disruptive day.

And just so you're aware of the scale of the disruption that one his companies, Tesla, has brought to the automotive industry, understand that it is now worth more than the following companies:

Toyota
Ford
Daimler-Mercedes
Volkswagen
BMW
GM
Fiat-Chrysler
Tata
Honda
Ferrari
Hyundai
Boeing
Airbus
American Airlines
Delta
Southwest
JetBlue

COMBINED.

Tesla is also worth more than
these pharma companies...

Novartis
Merck
AstraZeneca
BMS
Amgen
Sanofi
GSK

COMBINED.

And Mr Musk has certainly shown interest in this space on multiple occasions.

“In principle, I think synthetic RNA (and DNA) has amazing potential. This basically makes the solution to many diseases a software problem.”

ELON MUSK

JULY 2, 2020



“Tesla, as a side project, is building RNA microfactories for CureVac & possibly others.”

ELON MUSK

JULY 2, 2020



As you can see, Elon’s principal interest is in RNA, because it acts as a platform upon which further improvements are effectively a software rather than hardware problem. As you can imagine, many entrepreneurs will be interested in this.

Moderna's (Series G) investor pitch deck from 2017 proposed this software platform approach very clearly. A technology company is one which has negligible marginal cost for every product it produces or customer it serves, so you can see why this model is very attractive to the Silicon Valley Set.

If mRNA Could be a Drug... it Would be a Platform

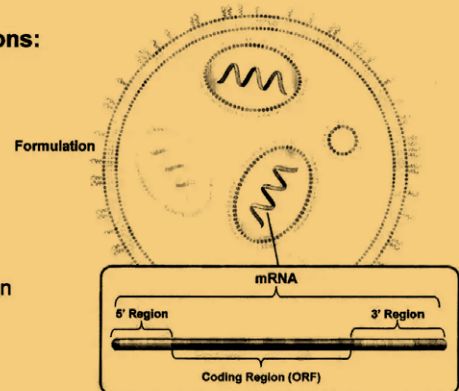
It would act like software; only the coding region varies from mRNA drug to mRNA drug

Within a given set of applications:

- Formulation = identical
- 5' Region = identical
- 3' Region = identical

Coding Region (ORF)

- Varies to encode for specific protein

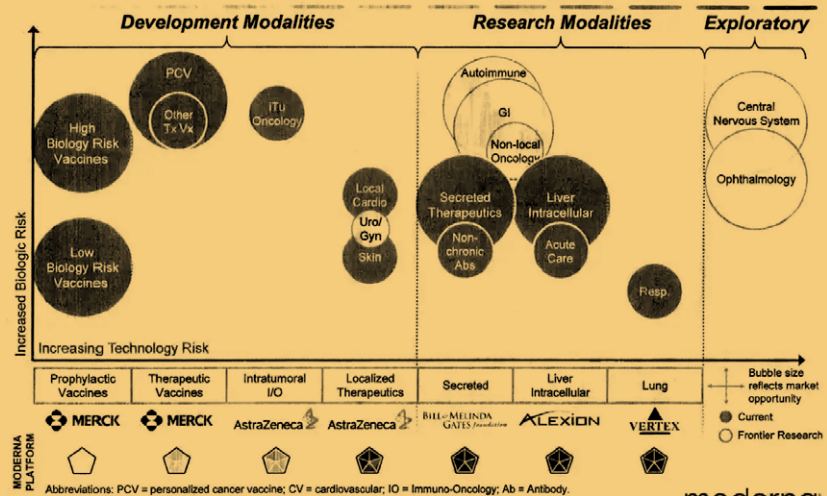


If mRNA works once, it should work many times

moderna

Moderna clearly saw vaccines as low-hanging fruit for mRNA, ie. low biological and technological risks combined with a large market opportunity:

As with Vaccines, Other Modalities' Target Space Will Expand as the Biology is De-risked



moderna

Covid-19 has provided a great proof-of-concept for mRNA; the fastest vaccines to achieve approval being provided by two companies which previously didn't have a single drug released between them.

Moderna is now developing an HIV vaccine based on the same technology, which entered early-stage clinical trials in 2021 with preliminary results expected in 2022. BioNTech, is working on mRNA vaccines for malaria, tuberculosis and also HIV, with trials expected to start this year. A new BioNTech-Pfizer partnership with Pfizer has just been announced to develop an mRNA Shingles vaccine.

Ugur Sahin and Ozlem Tureci, founders of BioNTech, are even more bullish. They made a prediction of their own in December:

“We believe that in 15 years, one-third of all newly approved drugs will be based on mRNA.

This technology is a potential turning-point in the pharmaceutical industry, comparable to the inauguration of recombinant DNA technology (allowing the production of human-protein drugs such as insulin), or monoclonal antibodies in laboratory fermenters, more than 40 years ago. The roll-out of this concept into readily available drugs promises to disrupt and transform the industry—and global health.”

UGUR SAHIN AND OZLEM TURECI
BIONTECH

Whether such a revolution is true or not, avoiding the usual complex and time-consuming fermentation processes in the production of many drugs has created a lot of interest, not just from within but also beyond our industry. Interestingly the diseases that these companies are now most advanced in - HIV, tuberculosis and malaria - are primarily responsible for deaths in lower-income countries, and Covid is providing useful incentive to set up manufacturing and distribution plants in developing countries, some of which have recently been agreed.

Will mRNA build a new marketplace in developing countries? Once the platform is established, will Elon Musk and others find it irresistible?



‘NO CODE’

BREEDS NEW

INTRA-

PRENEURS

AND PATIENT

PIONEERS

A commonly heard phrase in life science circles is: ‘it’s not about the technology; it’s about the people’. Which may well be true when trying to get digital solutions adopted in large corporations.

But when it comes to the solutions themselves, a certain level of technological understanding, or digital maturity, is required in order to be able to envision what’s possible. The problem is that there has always been a major divide between ‘techies’ and ‘business’, preventing a fluidity of creation and design.

Not anymore. A major wave of ‘no-code’ tools are redefining what’s possible when marketers, strategists, researchers and entrepreneurs build technical solutions without needing to write code. It’s the ultimate empowerment for the modern age.

Sitting here today, you might think it strange that business leaders would put together their own apps. But such statements have been proven wrong many times - remember how IBM predicted a worldwide demand for, maybe, 7 computers? Remember how until Microsoft Office became commonplace, you needed separate teams of word processors and tabulators? Remember how all design or video or graphics required experts and plenty of bureaucratic back-and-forth before anything could be created? Bringing the

act of creation into the person who is most motivated to do it actually allows more projects and iterations to be delivered in the first place, something Novartis realised when it announced a major partnership with Microsoft in 2019, designed to bring AI tools to every employee. Every employee? Yes.

Financial services companies have already been impacted significantly by no-code technology that allow employees to create and iterate solutions on the fly. For example a company called Unit21 helps the security teams at companies like Visa, eBay, Intuit and Coinbase create products that avoid fraud without having to go through developers first. Webflow now has 3.5m designers using its platform to generate bespoke websites and apps without requiring any coding knowledge.

And another motivated group of non-coders will be buoyed by these developments: patients. As we know there is already a growing biohacker movement, but no-code tools allow those with the imagination and passion to begin building themselves.

I, PATIENT:
THE RISE OF
SYNTHETIC
DATA

10

Getting quality, understandable, actionable, unbiased data is the most important and challenging part of any RWE effort and building any AI product today.

Synthetic data offers compelling advantages over the status-quo approach of collecting and labeling real-world datasets, especially when it comes to specialty or orphan disease where data is limited and extremely private.

There are many areas where limited datasets exist, not just in healthcare. To detect credit-card fraud, for example, researchers train AI models to look for specific patterns of known suspicious behavior, gleaned from troves of data. But unique, or rare, types of fraud are difficult to detect when there isn't enough data to support the algorithm's training. Likewise, car accidents or extreme driving conditions are rare, but self-driving cars will need to cope with these challenging conditions when they happen, so they must be simulated.

Using synthetic data is the key to really accelerating many arms of development, and it is a very different way of thinking about data. Synthetic data allows us to be much more open with information when sharing with partners and amongst different teams: there is nothing more private than data which has never existed in real life. It can also completely overcome bias or health equity concerns. As we tune the generation of data, we can create it at scale, and yet it still reflects reality.

We have worked with synthetic control arms for many years; proven to be very useful in cutting patient recruitment needs and overcome ethical issues of giving out placebos. But better advances in data creation also allows us to simulated disease sections of a population, modelling the TPP.

Gartner has predicted that by 2024, synthetic data will account for 60% of all data used in AI development across all industries. Facebook's acquisition of synthetic data startup AI.Reverie two months ago is a canary in the coalmine, while this year, multiple major computing platforms will launch new synthetic data efforts as they recognize the importance of this technology to tomorrow's AI stack and seek to attract more builders to their ecosystems, and soon the airwaves will be full of it.

Companies like Syntegra, MD Clone, Accenture and Phesi are early adopters of the technology, but I am most excited about Aetion's recent acquisition of synthetic firm Replica. Aetion has an ongoing close partnership with the FDA and may bring it a step closer to being accepted as a real metric to be used in trials. The movement begins at pace in 2022.

2022 Predictions

- 1 Pharma goes digital native
- 2 Amazon buys Teva
- 3 Biotech bursts
- 4 Pharma's reputation hits where it hurts
- 5 The beginning of the end for commercial teams in pharma
- 6 Nationalism as the path to health equity
- 7 Reimagining medicine: A psychedelic power trip
- 8 Elon Musk gets into pharma
- 9 'No code' breeds new intrapreneurs and patient pioneers
- 10 I, patient: The rise of synthetic data

Still reading?

If you've read this far, you're likely very interested in shaping our industry's future. And we'd like to get you involved. Send an email to Paul Simms on paul@impatient.health with the subject line 'predictor' and I will be sure to involve you in early conversations about 2023, when that time comes.

impatient

2022 Predictions

WRITTEN AND EDITED BY PAUL SIMMS

© PS DELTA LTD TRADING AS IMPATIENT HEALTH

JANUARY 2022
