

CREATING IP FOR IMPACT: THREE EPO CASE STUDIES

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Still at the early stages? Looking for funding? No proof of concept? Struggling to secure freedom to operate? Three EPO case studies review how intellectual property can lay a foundation for business ventures in one of the most complex fields of innovation: fighting cancer. In a book about how today's winners are lining up their IP, Thomas Bereuter and Ilja Rudyk from the EPO along with case study authors Adéla Dvořáková, Bowman Heiden, John McManus and Ciaran O'Beirne report

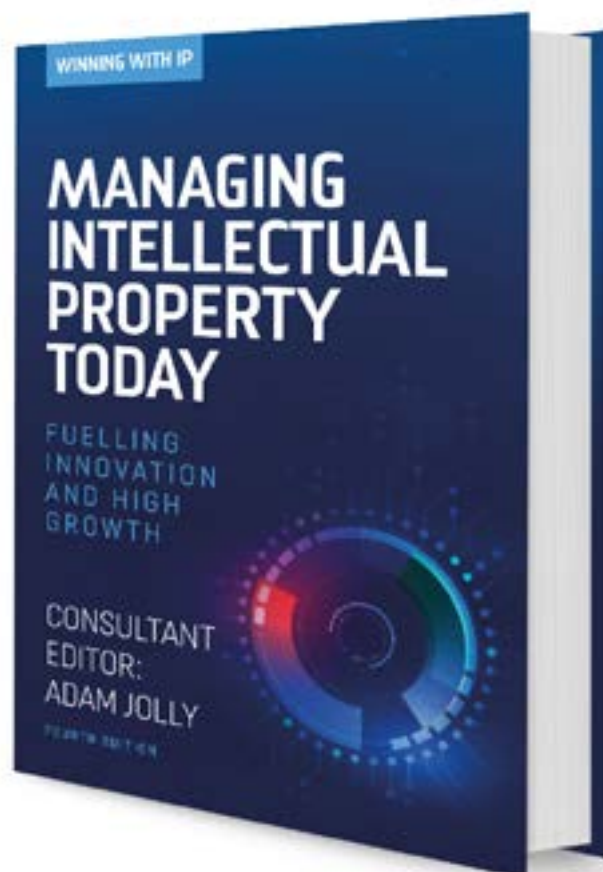
Finding cures for cancer is one of the toughest challenges in innovation. Novel ideas for treatments and diagnostics are hard to establish and slow to develop. Their effects, however, can be far-reaching for both society and the economy.

A clearer indication of whether breast cancer is likely to recur, for instance, could save up to 1.5 million women from undergoing the ordeal of chemotherapy each year. Or, as the World Health Organization argues, it could save up to 2.5 million lives by 2040.

At an individual level, anyone worried about having skin cancer can now obtain a diagnosis from a 3D probe in almost real time, instead of waiting 15 days for the results of an invasive biopsy. This adds up to a major saving in the efficiency and cost of medical treatments too.

Such improvements can only be achieved by a complex network of inventors, implementers, partners, users and funders. Intellectual property is what holds them all together at each delicate stage of an idea as it evolves and matures, enabling them to retain control and ultimately defining everyone's input and return.

In the early inspired stages of discovery, most concepts are usually far from market with little funding, no proof



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Growth is ever more centred on intellectual property. In tech. In innovation. In people. In disruptive models. In data. In value propositions. Those who integrate IP into their strategy, culture and mindset are significantly more likely to grow at pace. Drawing on the knowledge and experience of 20 leading IP players of today and tomorrow, including the high-growth team at the EPO's Patent Academy, this book gives a series of insights and lessons into how IP inspires and fuels growth of 10 percent, 20 percent, 50 percent and more, not just this year, but next year and into the future.

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and a diffuse outlook in terms of ownership. IP creates a solid basis by establishing the rights of the inventors and founders and how they can engage with business partners or users. In terms of cancer treatments, a core or platform patent is usually the first step, establishing exclusivity and securing time to develop and test the technology while exploring the market.

Options for the most promising uses are subsequently investigated, often resulting in more specific product patents down the value chain, as well as the accumulation of a portfolio around trade secrets, materials, prototypes and designs. As a product evolves between technology push and market pull, a new treatment will coalesce as a brand underpinned by a trade mark. Extra value is created at this stage too, with artificial intelligence used to track metrics on how a treatment performs and what can be improved next.

An overarching IP strategy will provide guidance and filter where, when and which IP rights to pursue, based on the venture's overall objectives. As it grows, a set of IP policies will be put in place and someone will take responsibility for overseeing the portfolio to make sure that the IP is proactively managed. Protocols around confidentiality and non-disclosure will be established early on, as well as how these requirements are communicated to fellow researchers.

At each funding stage, investors will check the robustness of an IP portfolio to protect their investment and whether the business is ready to scale up. Ultimately, it is the IP that will determine the venture's success and constitute its main source of value as an asset.

The following case studies from the EPO follow the path of three promising concepts to combat cancer. The case studies highlight how these concepts were managed over a cycle of ten to twelve years to create treatments and diagnostics that are already in use – or close to adoption – and starting to give genuine hope to millions of people at difficult moments in their lives.

As we will see, many inventors face a series of dilemmas as they progress. Should they bring in an additional partner or co-founder early on? What is the best stage to seek venture capital without diluting control or giving away too much? To what extent can the new treatment be adapted in the light of what may subsequently be discovered? How can inventors structure their venture to serve different markets? How can a venture stay independent and invest in the challenges of building its own sales? Is a trade sale the best way to ensure faster adoption of a new treatment? Leveraging IP gives inventors the agility to make all of these choices effectively and realise the full value of their innovation.

Damae Medical: building an IP culture

Detection of skin cancer is about to change. To date, doctors have first inspected any abnormalities with their own eyes, followed by a surface scan and a biopsy that can take up to 15 days to yield results. Most abnormalities are healthy, although delays in receiving the results can fray a patient's nerves and lead to higher medical costs. In some cases, however, cancerous abnormalities are missed altogether because they are hard to spot on the surface.

Now, a French spin-out is launching a diagnostic probe to scan 3D images of the skin that immediately reveal the full extent of the patient's condition. This will give patients immediate results and enable their doctor to offer more personalized care. In the worst-case scenario of surgery being required, only the affected tissue is removed and a follow-up operation is only carried out if absolutely necessary.

The technology for this probe originated at the Institut d'Optique in Palaiseau, where its potential was spotted by two students in photonics on their entrepreneurship programme in 2013. Together with the inventor, they launched a start-up called Damae Medical the following year with an exclusive licence for the core patent family jointly owned by their three partner institutions. Such a licence, while supportive in the short term, can give rise to challenges in terms of control later on. In 2019, Damae exercised its right to buy this foundational patent in return for equity.

It has since started several more patent families and is extending its range of IP as it moves from technology push to market pull. Damae Medical has also registered the design rights in its probe, along with several trade marks, and has safeguarded the copyright in its digital solutions.

With Damae's team now totalling 30 staff, its inventions are recorded and disclosed under the watch of a lead research engineer, 25 percent of whose time is spent on IP. Procedures are also followed to maintain confidentiality and care is taken to co-ordinate with Damae's active programme of scientific communication, managing disclosures to promote the technology and supporting freedom-to-operate by defensive publications in non-core areas.

Damae makes all of its own products, although it has two partners, which are at liberty to maintain and improve their own IP. Any improvements to the core technology, however, belong to Damae, which retains control over it.

By 2017, Damae was in a position to raise €2 million in seed funding, followed by a further €5 million in 2021.

It also won a €2.4 million EU grant to develop novel approaches to the non-invasive, personalised diagnosis of skin cancer.

In 2018, shortly before the launch of its 2D system, Damae found the agility of its IP put to the test with the discovery of a game-changing system for 3D stacking of images. Could it afford to pivot? How costly would a delay be?

It took the decision to switch all of its efforts to the 3D probe. Twelve months later, a protocol was ready and a patent filed. So far, Damae's probe, DeepLive, is being used in 40 hospitals worldwide, with more expected to follow.

Research in dermo-cosmetics is the other market that has emerged for Damae as a test for reactions to skin products. Up until recently, dermo-cosmetics accounted for half of Damae's total sales.

As a side effect of operating in more consumer-facing markets, Damae found itself using AI to track the metrics for all these projects, giving users a series of invaluable insights and creating a flow of ideas for Damae to pursue. It also plans to use AI to track the diagnosis of skin cancer, adding to the value that Damae can offer dermatologists and potentially identifying further areas for diagnostic improvements.

OncoQR: multi-modal IP

As a platform for stimulating the immune system to combat cancers and allergies, S-TIR has proved to be OncoQR's core technology platform supported by IP. The company OncoQR is now using S-TIR to map out several different treatment paths and has formed a joint venture for some cancer types, such as pancreatic cancer. While OncoQR is pursuing its own research in breast cancer, it is licensing S-TIR for use in neoepitopes generated by mutant cancer genes.

Essentially, S-TIR solves one of the outstanding challenges in immunology: how antibodies can attack unhealthy cells without provoking an over-reaction. For Geert Mudde, originally an immunologist at Novartis, the solution was modular: create a warhead to carry the immunogen to the target cell, whether it be cancerous or allergic.

He was lucky enough that Novartis decided to abandon the technology in its infancy, which allowed him to develop it further. Originally, he filed a patent in 2006 after leaving Novartis. In 2010, he spun out the IP into a separate venture, S-TARget therapeutics, and brought in a biotech engineer with business experience, Christof Langer, as a co-founder

to develop the venture. They have since been granted two further patents on the platform.

The first tests on allergies were highly promising. At this point, the founders decided to pursue a twin track for the venture: in cancers and in allergies.

At OncoQR for cancer, they have used their IP in a combination of models to recruit partners that will research S-TIR's use for different cancer types. This has led to two product patents to date: for pancreatic cancer as a joint venture and for breast cancer as OncoQR.

In their partnerships, know-how about the most efficient production techniques is included in any agreements as trade secrets. Any improvements in the platform technology are then licensed back to OncoQR, effectively creating a mechanism for open innovation, which has resulted in several improvements to the warhead that are also made available to all licensees.

The flexibility of these different models has allowed OncoQR to fund much of its own research through IP licensing revenues, alongside public national grants. So far, its founders have sought to retain full control over their IP and have been wary of talking to venture capitalists too early. For now, although they remain open to all options, they prefer to use their IP to talk to pharmaceutical companies about building on their progress and moving into clinical trials.

OncoMark: serial IP entrepreneurs

Better diagnosis and prognosis of cancer was the inspiration for creating OncoMark, a spin-out company established at University College Dublin (UCD). In 2021, OncoMark was acquired by a leading US molecular diagnostic company. The management and investors in OncoMark have now reinvested some of the proceeds from the acquisition to set up a start-up to investigate further use of biomarkers with other cancers, such as prostate cancer and melanomas. This follow-on combines the talents of a UCD professor of biology, William Gallagher, and a veteran of the diagnostics industry, Des O'Leary.

After starting his career at a French pharmaceutical company, Rhone-Poulenc, later Sanofi-Aventis, Professor Gallagher brought an interest in translational research to the university. He set up his original venture, OncoMark, in 2007 where he built up a team to explore biobanks for diagnostic purposes.

The potential for using biomarkers to make better informed treatment decisions for breast cancer emerged from Gallagher's research with a colleague at Trinity College

Dublin. If we can better predict the likely recurrence of cancer, they asked, can we avoid chemotherapy and the associated side effects for two-thirds of women who are diagnosed with a specific subtype of breast cancer and who do not require and/or benefit from chemotherapy?

Research into this question generated interesting findings and the two universities were sufficiently convinced to file a priority patent with the EPO to protect the invention. To de-risk and validate the patented technology, the universities licensed the invention to OncoMark. It, in turn, applied for a €2.7 million grant from the EU and raised a further €2.1 million from an Irish investment syndicate.

In 2015, Des O’Leary joined as chief executive, switching the company’s strategic focus from research to development. The prognostic test gained a CE mark and was trade marked. Terms were also agreed with a manufacturing partner and the packaging was prepared for the product launch.

In the meantime, Cepheid, a leading molecular diagnostics company had spotted the test, which it thought could strengthen its own existing oncology portfolio. The dilemma for OncoMark’s owners was whether to invest in the challenges of building their own sales and distribution channels or opt for rapid adoption with Cepheid. In the end, they decided to accept Cepheid’s offer of a significant investment to further develop and clinically validate the test on Cepheid’s GeneXpert platform before the acquisition was completed in 2021.

For Gallagher and O’Leary, the cycle of commercializing IP is now starting all over again. They have decided to invest the proceeds from their share of the sale in a new diagnostics start-up, OncoAssure, to investigate the potential of biomarkers with other cancers.

IP pointers

Each of these case studies draws on the insights and experiences of multiple actors in turning cancer discoveries into treatments and diagnostics for patients. Taken together, their experiences and insights give a series of IP pointers about what matters when creating ventures that can make an impact in the clinic. These options and lessons are covered in depth by each of the EPO’s case studies. Here are some of the highlights:

- IP gives you the agility to adapt your business strategy as you improve your invention and explore how it is going to be used.

- Founders who combine a background in both research and industry often set their sights early on creating an IP venture by engaging with users and collecting test data.
- A core patent establishes priority for your invention and gives you time to explore its use before deciding how and where to extend it.
- A spin-out or start-up consolidates the IP in one place. It can then capture any more IP that is created, guarding against dilution when engaging with partners or funders.
- A co-founder is often involved to help build the commercial case either in the early stages or as the treatment moves beyond proof of concept.
- Ventures often begin by exclusively licensing their core inventions from their parent institutions, whether academic or corporate. In the short term, it has advantages of continuing cooperation, but can cause challenges with control later, so an option to purchase the IP is often exercised.
- As innovations move from technology push to market pull, the range of IP broadens to include trade secrets protecting know-how, designs and copyright. As a brand strengthens, trade marks become one of the principal sources of a venture’s value.
- AI is opening up insights into a much wider range of metrics about how treatments are being used. Any resulting new and inventive solutions with a technical effect can be patented.
- An IP strategy, often under the direction of the chief scientific officer, allows you to prioritise which IP rights to pursue and where.
- Tracking and recording further inventions and improvements usually becomes the responsibility of someone in or close to the research team, who will also monitor confidentiality and disclosure.

- All this IP creates the potential for several different commercialization models: you can continue your own research and development, collaborate, license, form a joint venture or sell the technology. For a platform technology, you may well combine a version of all of these models in different niches.
 - You can opt for three main types of licence for your technology: for the platform, for a product or for non-commercial research. Your licence will have more value when you can include a rich mix of IP, including know-how and additional R&D support.
 - With your partners, you might decide that you will each be free to create your own IP, but encourage a culture of open innovation to improve the core technology, often through back-licences. In any case, securing freedom to operate is essential.
 - Early on, research grants are a significant source of funding. Licensing your technology to secondary markets or for different fields of application is often an effective way to fund ongoing research too.
 - With venture capital, it is worth getting your timing right. It is usually best after proof of concept but before you lose momentum when running out of money or patent lifetime becomes an issue.
 - If a pharmaceutical company takes a serious interest in your IP, it is likely to fund some clinical proof first. If it then offers to acquire the technology, you will have to decide whether the offer is worth accepting or if it is better to invest in building your own sales operation.
 - Advisory boards with views from both science and business can help to map out the series of IP and financing decisions that ventures will face.
- *Any opinions expressed in this article are those of the authors and not necessarily those of the European Patent Office or the authors' respective organizations.*

For the full versions of the series of case studies published by the EPO about managing IP in transformative innovations for cancer, see epo.org/case-studies.

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