



Oncode Institute

*Outsmarting cancer
Impacting lives*

Annual Progress Report

Period Jan/2021 - Dec/2021

Reporting Period 4

Contents

1. Acronyms and abbreviations.....	3
2. Oncode at a glance.....	4
2.1 Vision & Mission.....	4
2.2 Executive Summary.....	5
2.3 Nederlandse samenvatting	6
3 Scientific Excellence, Collaboration & Valorization.....	9
3.1 Scientific excellence	9
3.1.1 Base funding	9
3.1.2 Our facilities, world-class science.....	11
3.1.3 Technology Access	13
3.1.4 Interview Laura Heitman & Jop Kind	14
3.2 Collaboration.....	16
3.2.1 Meeting people during the COVID-19 pandemic	16
3.2.2 Patient Engagement.....	17
3.2.3 Public Private Partnerships	19
3.2.4 Oncode Accelerator Projects	21
3.2.4 Interview with Bas van Steensel.....	22
3.3 Valorization	24
3.3.1 Impact of Technology Development fund.....	25
3.3.2 Achieving Proof of Concept.....	26
3.3.3 Oncode Oncology Bridge Fund.....	28
3.3.4 Oncode Strategic funding support	30
3.3.5 Affordable Health Care programme.....	31
3.3.6 Interview Madelon Maurice.....	35
4. Governance and Management.....	38
5. Management Report	41
6. Key Performance Areas	47
Appendix I.....	51
Appendix II.....	54
Appendix III.....	62
Appendix IV.....	69

1. Acronyms and abbreviations

AHC	Affordable Health Care
CAB	Clinical Advisory Board
CPoC	Clinical Proof-of-Concept
CRUK	Cancer Research UK
EIR	Entrepreneurs-in-Residence
ERC	European Research Council
EZ	Dutch Ministry of Economic Affairs and Climate Policy
FAIR	Findable Accessible Interoperable Reusable
HUB	Hubrecht Organoid Technology
IAB	International Advisory Board
IE	Industry Engagement
IP	Intellectual Property
IRC	Independent Review Committee
I & T	Infrastructure & Technology
IMI	Innovative Medicines Initiative
KWF	KWF Kankerbestrijding (Dutch Cancer Society)
KNAW	Koninklijke Nederlandse Akademie van Wetenschap (Dutch Royal Academy of Arts and Sciences)
OCW	Dutch Ministry of Education, Culture and Science
NFU	Nederlandse Federatie van Universitair Medische Centra (Dutch Federation of University Medical Centers)
NKI	Netherlands Cancer Institute
NWO	Netherlands Organization for Scientific Research
OEDES	Oncode Exploratory Development Expert Support team
OSFD	Open Science and FAIR Data
OI	Oncode Investigator
PMC	Princess Máxima Center for Pediatric Oncology
R & D	Research and Development
RMC	Research Management Committee
SB	Supervisory Board
SMEs	Small and Medium-sized Enterprises
SRL	Socially Responsible Licensing
TKI	Topconsortia for Knowledge and Innovation
TA	Technology Access
UMC	University Medical Center
VIB	Vlaams Instituut voor Biotechnologie (Flemish Institute for Biotechnology)
VITAE	Valorization in Training and Education programme
VWS	Dutch Ministry of Health, Welfare and Sport
ZonMw	Netherlands Organization for Health Research and Development

Annual Progress Report

2. Oncode at a glance

2.1 Vision & Mission

Our Vision

To crack the code of cancer for a future in which everyone can survive cancer with the best possible quality of life.

Our Mission

To accelerate breakthrough discoveries and speed up their translation into new diagnostics and treatments for cancer patients.

Our mission is built on 3 pillars:

Scientific Excellence

Pioneering basic science is essential for increasing our understanding of the origins, progression, and vulnerabilities of cancer. We invest in high-risk, high-impact, basic research and state-of-the-art technologies, paving new roads towards developing transformative therapeutic strategies.

Collaboration

The challenges of cancer push us to go beyond the competitive model of science. We are a multi-disciplinary and collaborative community of world-class oncology researchers across the Netherlands. We work together in national and international partnerships with leading scientists, clinicians, and innovative companies, as well as patients, charities, and research institutions.

Valorization

A dedicated team of experts proactively identifies promising new inventions and facilitates their development into novel therapeutic and diagnostic approaches. With dedicated funding, we invest in translational and clinical research, public-private partnerships, and establishing new ventures. This accelerates the translation of breakthrough discoveries into tangible benefits for patients and society at large.

2.2 Executive Summary

Oncode is founded on 3 pillars: Scientific Excellence, Collaboration, and Valorization – together creating impact. 2021 marked the fourth year of Oncode's operations, during which the institute was able to capitalize on activities initiated in previous years while simultaneously preparing itself for the next phase of Oncode. Like 2020, the past year was also marked by the ongoing pandemic. In 2021, research activities could largely be carried out under 'normal' conditions, but social distancing regulations heavily impacted the ability to meet and interact with people face to face.

Last year, Oncode received a very positive assessment by the organization's International Review Committee (IRC). This was a crucial milestone that needed to be achieved before Oncode could start drafting its phase 2 strategic plan and initiate discussions with its funding partners and partner institutes to reach agreement on the accompanying phase 2 budgets and agreements. In 2021, Oncode also conducted an assessment of those Oncode Investigators (OIs) who were due for their 5-year review, through a fair and transparent process. In early 2022, the IRC assessed Oncode's strategic & financial plan and the OI assessment, bringing Oncode another step closer to its next 5 years of operation. While preparing for Phase 2, business continued within Oncode's research groups and the Oncode teams supporting Oncode's targeted programmes and valorization activities.

2021 proved to be a productive year both scientifically and collaboratively, as well as in terms of Oncode's efforts to translate research findings towards impact for patients. Oncode's efforts to create an environment in which Oncode researchers can reach their maximum innovation potential are supported by offering Oncode Investigators (OIs) virtually unrestricted base funding so they have the freedom to explore new ideas. In this way, Oncode promotes highly innovative basic and pre-clinical research. Examples of the impact resulting from these base funds are showcased in section 3.1.1. Through its Infrastructure & Technologies (I&T, section 3.1.2) programme, Oncode also ensured accessibility to key research capabilities. Furthermore, Oncode initiated the new Technology Access programme (section 3.1.3) in 2021, aimed at providing the Oncode community with early access to emerging technologies that are potentially of high value to Oncode research.

Like last year, the ongoing effects of the COVID-19 pandemic forced Oncode to adapt the wide variety of meetings and events it normally holds to promote interdisciplinary research. During certain periods of the year when COVID restrictions were relaxed, face to face meetings could be organized. However more often than not, hybrid or fully-digital meetings were organized to maintain interactions between researchers, clinicians, patients, and industry (section 3.2.1). Oncode's Patient Engagement programme (section 3.2.2), which was set up to promote interaction between researchers and (ex)patients, gained real traction in 2021. Furthermore, Oncode continued to stimulate interaction with private organizations to enable the efficient translation of research findings. Oncode's efforts to facilitate and support these interdisciplinary collaborations have led to a wide range of impactful projects and initiatives, some of which can be found in section 3.2.3. Lastly, in preparation for its phase 2 strategy, Oncode rolled out a new initiative called the Oncode Accelerator Projects (OAP) programme (section 3.2.4) to support large-scale interdisciplinary research projects.

Oncode's overarching valorization strategy is aimed at accelerating the translation of new research innovations into tangible applications for patients and society. To achieve this, Oncode's international team of business developers provides proactive valorization support to all OIs. In addition, Oncode's dedicated valorization funds enable the valorization team to swiftly 'change gear' and act on newly arising opportunities. In 2021, the valorization team exceeded the annual targets set at the beginning of Oncode with regard to setting up agreements, new invention disclosures, patent filings, and spin-off companies (section 3.3 and Appendix II Oncode Output).

Oncode's TechDev fund (section 3.3.1) efforts also bore fruit with several new collaborations, spin-offs, and clinical projects de-risked through TechDev fund investments. The Clinical Proof-of-Concept programme (CPoC, section 3.3.2) was also used to de-risk new research findings and demonstrate the potential diagnostic or therapeutic value of research findings in a clinically relevant setting. For the first time, 2021 also marked the year that a newly developed 'Oncode' therapeutic was clinically tested in a phase 1 trial. In 2021, the Oncode Oncology Bridge fund (section 3.3.3) also continued to provide pre-seed and seed capital to commercially viable enterprises emerging from the Oncode community. Two new spin-offs were launched in 2021, bringing the total to 7.

Lastly, Oncode applies several of its programmes and funds to contribute to the affordability of healthcare (AHC). This includes funding CPoC projects focused on repurposed/off-patent drugs or personalized medicine through the Drug Repurposing programme. Oncode also contributes to AHC by ensuring that socially responsible licensing guidelines are applied to all relevant licenses (section 3.3.5).

2.3 Nederlandse samenvatting

Oncode Institute is opgericht met ambitieuze doelen: het stimuleren van excellent fundamenteel onderzoek, het inspireren en bevorderen van samenwerking en een efficiënte vertaling van onderzoek naar betere en meer betaalbare zorg voor patiënten. In dit vierde 'Oncode' jaar kon het instituut de vruchten plukken van de activiteiten die in voorgaande jaren waren gestart, tegelijkertijd werden voorbereidingen getroffen voor de volgende fase van Oncode. Net als 2020 stond ook het afgelopen jaar in het teken van de aanhoudende pandemie. In 2021 konden de onderzoeksactiviteiten gelukkig grotendeels onder "normale" omstandigheden worden voortgezet, maar de nationale Corona maatregelen hadden een grote invloed op het organiseren van kleine en grote bijeenkomsten.

Vorig jaar behaalde Oncode een belangrijke mijlpaal met de positieve beoordeling van Oncode's Internationale Review Commissie (IRC). Deze cruciale mijlpaal moest worden behaald vóórdat Oncode kon beginnen met het bouwen aan haar tweede fase. In 2021 is een nieuw strategisch plan geschreven voor de komende 5 jaar. Ook zijn er gesprekken gevoerd met financiers en partnerinstellingen om het budget en andere afspraken vast te leggen. Daarnaast voerde Oncode de evaluatie uit van alle Oncode-onderzoekers die aan hun vijfjaarlijkse beoordeling toe waren, via een eerlijk en transparant proces. Begin 2022 beoordeelde de IRC het strategische & financiële plan van Oncode, inclusief het proces en de uitkomst van de onderzoekers-evaluatie. Terwijl deze voorbereidingen voor de tweede fase werden getroffen, gingen de

lopende zaken gewoon verder, in de labs van de Oncode onderzoekers en binnen de verschillende Oncode teams die zorgdragen voor de ondersteunende programma's, activiteiten en budgetten.

2021 bleek een productief jaar te zijn, innovatief onderzoek leidde tot top publicaties, nieuwe onderzoeksfinancieringen en samenwerkingen. Ook Oncode's inspanningen om onderzoeksresultaten te vertalen naar impact voor patiënten en maatschappij waren succesvol. Binnen Oncode krijgen onderzoekers wetenschappelijke vrijheid, dat wil zeggen dat ze mogen pionieren om nieuwe kennis op te doen. Hiervoor hebben Oncode onderzoekers beschikking over zowel financiële middelen, een vrij te besteden *base fund*, als de benodigde technologische middelen. De *base funds* bevorderen innovatief fundamenteel- en preklinisch onderzoek van hoge kwaliteit, dat niet met reguliere financiering kan worden gerealiseerd. In sectie 3.1.1 zijn verschillende voorbeelden te vinden van de impact die de *base funds* maken. Daarnaast ondersteunt Oncode verschillende *hoogwaardige onderzoeksfaciliteiten* die niet alleen beschikbaar zijn voor de Oncode gemeenschap, maar voor heel Nederland (sectie 3.1.2). Oncode heeft in 2021 het nieuwe *Technology Access-programma* (sectie 3.1.3) opgestart, dat erop gericht is de Oncode gemeenschap vroegtijdig toegang te geven tot nieuwe opkomende technologieën die potentieel van grote waarde kunnen zijn voor Oncode onderzoek.

Door de aanblijvende gevolgen van de COVID-19 pandemie was Oncode genoodzaakt om de bijeenkomsten en evenementen aan te passen. Wanneer de nationale Corona maatregelen het toe lieten, zijn er 'live' bijeenkomsten georganiseerd. Oncode moest helaas nog vaak terugvallen op hybride of volledig digitale bijeenkomsten om de interacties tussen onderzoekers, klinici, patiënten en de industrie te stimuleren en in stand te houden (sectie 3.2.1). Het *Patient Engagement programma* van Oncode (sectie 3.2.2), opgezet om de interactie tussen onderzoekers en (ex-)patiënten te bevorderen, kreeg in 2021 weer meer voet aan de grond. Daarnaast bleef Oncode de interacties met partners uit het bedrijfsleven stimuleren om de efficiënte vertaling van onderzoeksresultaten naar de kliniek te faciliteren. Dit heeft geleid tot een breed scala aan mooie projecten en initiatieven (sectie 3.2.3). Ten slotte heeft Oncode, als onderdeel van haar fase 2-strategie, een nieuw initiatief gelanceerd: *de Oncode Accelerator Projecten* (sectie 3.2.4). Met deze projecten wil Oncode grootschalige interdisciplinaire onderzoeksprojecten stimuleren en ondersteunen.

Oncode's valorisatiestrategie is gericht op het versnellen van de vertaling van nieuwe onderzoeksresultaten naar toepassingen voor patiënt en maatschappij. Om dit te bereiken, biedt Oncode proactieve valorisatie-ondersteuning aan haar onderzoekers. Een internationaal team van *business developers* kan snel handelen dankzij de toegang tot de verschillende speciale valorisatiefondsen van Oncode. Daarmee kunnen ze effectief inspelen op nieuwe kansen en mogelijkheden. In 2021 werd de jaarlijkse doelstelling van het valorisatieteam ruimschoots overtroffen. Zo sloten zij meer overeenkomsten af met private partners, zijn er meer patenten en octrooiaanvragen ingediend, meer licenties afgesloten en lanceerde het met succes twee nieuwe spin-off bedrijven (sectie 3.3.3 en bijlage II Oncode Output). Dit jaar besteden we ook aandacht aan de inspanningen van Oncode's *TechDev-fonds* (sectie 3.3.1), investeringen uit dit fonds hebben geleid tot verschillende nieuwe samenwerkingsverbanden, spin-offs en klinische projecten waarvan de risico's dankzij de investeringen van het TechDev-fonds zijn verminderd. Het programma voor *klinische proof-of-concept* (CPoC, sectie 3.3.2) gebruikt Oncode om het risico van nieuwe onderzoeksresultaten te verkleinen en de potentiële diagnostische of therapeutische waarde van

onderzoeksresultaten in een klinisch relevante setting aan te tonen. 2021 was ook het jaar waarin, voor het eerst, een nieuw ontwikkeld "Oncode"-therapeutisch middel klinisch werd getest in een fase 1-studie.

Oncode draagt daarnaast bij aan de betaalbaarheid van de gezondheidszorg. Hiertoe heeft Oncode er onder meer voor gezorgd dat de "*maatschappelijk verantwoorde licentierichtlijnen*" werden toegepast op alle relevante licenties en stelt het ook met succes haar *drug repurposing library* ter beschikking aan de wetenschappelijke gemeenschap (sectie 3.3.5.).

3 Scientific Excellence, Collaboration & Valorization

3.1 Scientific excellence

Oncode was founded on the firmly held belief that innovations in oncology stem from discoveries in basic science, such as a better understanding of cancer cell biology, evolving cancer ecosystems, and cancer-tissue interactions. Within Oncode, more than 900 outstanding scientists from 61 research groups across the Netherlands, all specialized in the field of basic oncological research, are united through a shared mission and strategy. The Oncode ecosystem builds upon the excellent research ecosystems already present at our partner institutes, through which Oncode is able to connect to additional expertises, facilities and networks.

Oncode challenges its investigators to initiate ‘high-risk, high-gain’ research lines by providing them with substantial, near-unrestricted ‘base’ funding. Additionally, Oncode has set up advanced new technologies, infrastructures, and dedicated Oncode facilities to support high-quality research. It also facilitates training and mentoring activities.

3.1.1 Base funding

Base funding 101: Oncode promotes the innovation potential of its research community by providing its investigators with base funds. Oncode base funds are near-unrestricted and are designed to promote innovative basic and pre-clinical research lines of high quality (high-risk/high-gain) research, or for OIs to apply their expertise in new research fields. Typically, these research lines are difficult to finance in the standard funding landscape due to a lack of preliminary data or an adequate track record and limited funding availability. Of equal importance, Oncode’s base funds provide OIs with the financial capability and flexibility to accelerate research lines, change the scope of research programs, or quickly terminate non-successful projects. The impact of Oncode’s base funds can be seen on multiple levels, of which three – publications, new funding opportunities, and the ability to venture into new research and collaborations – are highlighted below.

Publications: In 2021, OIs collectively published 443 unique publications, 6 of which were in the journals *Nature*, *Cell* or *Science*. Of these publications, 78% were Open Access publications and 15% were co-authored by at least one other OI. 2021 was a productive year, with great publications build on the research performed by our OIs in our partner institutions and while not all these publications can be attributed to Oncode’s efforts, Oncode is now seeing the first publications for which the availability of Oncode base funding was vital. Several notable examples of key publications from the Oncode community are listed below.

- Jin et al., **Nature** (2021). Study by the *Bernards* and *Akkari* groups showing meaningful clinical responses in patients with advanced hepatocellular carcinoma upon treatment with combination of lenvatinib plus gefitinib.

- Bollen et al., **Nature Genetics** (2021). Study by the *Snippert, Kops, Cuppen* and *Lens* groups presenting the 3D Live-Seq protocol, which integrates live-cell imaging of tumour organoid outgrowth and whole-genome sequencing, enabling the reconstruction of evolving tumour cell karyotypes across consecutive cell generations.
- Geijer et al., **Nature Cell Biology** (2021). Study by the *Marteijn, W. Vermeulen* and *Bernards* groups showing the role of ELOF1 in transcription-coupled nucleotide excision repair, thereby protecting the transcription machinery from DNA damage.
- Van Neerven et al., **Nature** (2021). Study by the *L. Vermeulen* and *JP Medema* groups using organoid technology and the application of lithium, leading to the discovery of how the chance of polyps forming in the intestine, and thus the development of colorectal cancer, can be reduced.
- Van de Haar et al., **Nature Medicine** (2021). Study by the *Voest, Cuppen* and *Wessels* groups demonstrating that there is limited evolution of the actionable genome of treated metastases, providing evidence that a single whole-genome sequencing analysis of a metastatic biopsy is generally sufficient to identify genomic biomarkers and identify investigational treatment opportunities.

Bas van Steensel (NKI): *“The base funding of Oncode provides the flexibility that is essential for dynamic, creative, and high-risk research, which is not easily fundable in conventional grant schemes, unless major amounts of preliminary data are generated. Oncode makes it possible to conduct proof-of-principle studies and generate these preliminary data.”*

Miao Ping Chien (Erasmus MC): *“We have applied FUNseq to profile invasively migrating glioblastoma cells and identified a key driving pathway. The project required a multidisciplinary team and with Oncode’s funding I was able to gather a team with diverse backgrounds, including a multidisciplinary PhD student (the project lead) to conduct this project, because bioinformatics, molecular biology and biotechnology experience were needed.”*

Sarah Derks (Amsterdam UMC): *“The innovative aspect of this project lies in studying Tumour Lysis Syndrome in gastric cancer and using digital spatial profiling as a methodology, which will provide us with an immune characterization with unprecedented detail. Because KWF did not want to fund the project without preliminary data, Oncode base funding allowed us to start the project.”*

New funding opportunities: Oncode’s Base funds enable OIs to initiate new research lines and gather preliminary data on promising new findings. In 2020, Oncode had already noticed that ‘base fund’ research lines resulted in many successful national and international grant applications. This trend continued in 2021; our investigators have reported 18 awarded grant applications based on results obtained through using base funding, with a total budget of €18.2M (see appendix II). Additional grant applications are pending a decision. Notable grant applications include those by:

- **Peter ten Dijke** (Leiden UMC) – ZonMw Open Competition grant, €750K
- **Jarno Drost** (PMC) – NWO VIDI grant, €800K

- **Sylvie Noordermeer** (Leiden UMC) – KWF, €750K
- **Michiel Vermeulen** (Radboud University), **Jop Kind** (Hubrecht) – NWO-consortium grant, €3.5M
- **Linde Meyaard** (UMC Utrecht) – industry grant €175K

***Jop Kind** (Hubrecht Institute): “Our Oncode base fund allowed us to develop the method further to generate proof-of-concept. Based on these pilot experiments, we have now secured funding from a KNAW research fund (€250K) to further develop this project in collaboration with Jan Paul Medema.”*

***Monique Den Boer** (PMC): “We used the Oncode base fund to pioneer with these types of immunotherapeutic/niche studies, generating (pilot) data to gain expertise and show proof-of-concept for this innovative field of research. In 2021, additional funding has been secured (ODAS grant, €355K) for this research.”*

***Wim Vermeulen** (Erasmus MC): “Obtaining funding for C. elegans research is intrinsically challenging within the Dutch funding landscape. However, through base-fund enabled results we acquired two C. elegans-associated research grants (ENW ECHO grant, €274K and ENW, ALW-open grant, €295K).”*

Recognition: awards and memberships: In addition to the publication of high-quality papers and grants, OIs receive (inter)national recognition through nominations for awards and invitations for membership of specific scientific communities. These awards and memberships reflect the quality and relevance of the recipient’s research achievements. As in previous years, multiple OIs received (inter)national recognition in 2021. Notably, this was not limited to senior members of Oncode’s research community. Junior group leaders and Postdoc researchers also received recognition in this way, examples of which can be found below:

- **Ammodo Science Award** - Louis Vermeulen (Amsterdam UMC)
- **International Birnstiel Award** - Sanne Boersma (Hubrecht Institute, Tanenbaum Group) and Sanne van Neerven (Amsterdam UMC, L. Vermeulen Group)
- **Jeantet Collen Prize for Translational Medicine** - Ton Schumacher (NKI)
- **EMBO membership** – Wim Vermeulen (Erasmus MC), Karin de Visser (NKI)
- **Prix Galien excellence award** – Marvin Tanenbaum & Wouter de Laat (both Hubrecht Institute)

3.1.2 Our facilities, world-class science

Infrastructure & Technology 101: Over the years, Oncode has invested almost €10M in research infrastructure via its Infrastructure and Technology (I&T) programme, providing the Oncode community and other scientist at our partner institutes with access to state-of-the-art technologies, infrastructures, and facilities. The programme has so far allowed Oncode to fund 10 infrastructure projects and set up 7 state-of-the-art research facilities for the Oncode and wider Dutch research community, thereby supporting broader access to key scientific capabilities that are more cost effective when shared. To ensure optimal exposure and usage of infrastructure and research facilities, Oncode frequently organizes technical masterclasses and workshops, and actively communicates about them through various media channels.

While Oncode did not make any new I&T investments in 2021, the programme remained active to promote Oncode's existing facilities, technologies, and infrastructure. It did so through various communication channels, meetings, and the [Oncode website](#), and through the organization of 4 technical [workshops](#) to showcase the available expertise and technical capabilities of the various facilities. The workshops also provided an opportunity for hands-on support by technical experts for specific Oncode projects. The combination of high-end facilities and tailor-made masterclasses enables the Oncode community to optimally use the scientific and technical capabilities present in Oncode to answer scientific questions, often in collaboration with other Oncode groups that possess the required expertise (for example, the GPU infrastructure). Oncode's I&T facilities are also accessible to outside users, with several now being used by private organizations on a fee-for-service basis.

Hans Clevers (Hubrecht Institute): "We applied the Oncode drug repurposing library with over 5,600 compounds on different tumour organoid lines derived from HNSCC. [...]. This allowed us to select 100 highly promising compounds that effectively reduced tumour cell numbers in at least two tumour lines, while leaving the non-malignant control line unaffected."

Scenic Biotech: "Scenic Biotech has made use of the excellent Oncode protein facility [...] The dedication and technical knowledge of the protein production team is impressive, which resulted in successful projects. We look forward to maintaining our productive collaboration."

Monique den Boer (PMC): "We are very pleased with the cooperative mindset of the Single Cell Sequencing facility of the Van Oudenaarden lab. Their input in our experimental design and the received dataset are both of high quality and the facility is also very accessible for any question related to the next steps in data analysis. This facility is a showcase of how to open up specific, highly innovative technologies for a broader community."

The Oncode single-cell (epi)genome sequencing facility: The Oncode '[Single-Cell Core](#)' became operational in 2019 with the goal of setting up a facility for DNA analysis at the level of individual cells, both for genomic DNA sequencing as well as epigenetic measurements. The facility is now fully operational, and a masterclass was organized in early 2021. During 2021, the facility processed 242 samples from 23 different research groups from 10 different institutes from 4 different countries. In total, 11 different Oncode research groups made use of the facility in 2021.

Oncode Therapeutic Antibody Facility: As part of the I&T programme, Oncode initiated a collaborative project together with OI Linde Meyaard (UMCU) and Jeanette Leusen (head of the Utrecht Monoclonal antibody Facility (UMab)) with the goal of offering OIs the opportunity to produce high quality antibodies (targeted against membrane proteins). Within the [Therapeutic Antibody Facility](#), technical experts work closely with researchers to develop new monoclonal antibodies potentially suited for clinical applications. The facility employs a new, unique, and very efficient cellular immunization method in mice, through which antibodies can be raised against (for example) low immunogenic membrane proteins. In addition, this facility can make antibodies against conformational epitopes and generate agonistic and antagonistic antibodies. Since the inception of the Oncode programme in 2020, 6 project proposals from Oncode have

been submitted for antibody generation. Of these, two projects have been granted and are currently under development. Two additional projects are funded through either the TechDev or external funds.

UFO Biosciences: This new Oncode facility, launched in 2021, offers services to microscopically screen cell populations and identify cells of interest based on imageable phenotypes, with the aim of isolating and profiling cells of interest. Using functional single-cell sequencing (FUNseq) technology originating from the Chien lab (Erasmus MC), the [UFO Bioscience facility](#) helps researchers target cells that are of interest based on (a combination of) their dynamic behaviour, molecular identity, or imageable characteristics. While the I&T programme did not provide funds for UFO Biosciences, Oncode enabled its establishment through multiple channels. The Oncode business development team, together with the Erasmus MC Technology Transfer Office (TTO), helped OI Miao-Ping Chien to develop a strategy for offering the technologies she developed in her lab as a service. Additionally, through Oncode’s TechDev fund (see section 3.3.1) the technology was further developed to be more broadly applicable. With funding from the Josephine Nefkens Stichting, the facility became operational in 2021. Oncode and Erasmus MC provide UFO Biosciences with access to a broad network of potential future customers, investors, and strategic partners. UFO Biosciences closely collaborates with the Oncode [Single-Cell Core facility](#) and the Oncode spin-off company [Single Cell Discoveries](#).

Miao-Ping Chien (Erasmus MC): *“Oncode has successfully assisted me in setting up the UFO Biosciences facility, aiming to offer our single-cell screening and FUNseq technology to researchers and clinicians at Erasmus MC and the Oncode community. With this, we were able to connect with and help more researchers and clinicians. Currently, we are evaluating the spinoff opportunity based on our patented technology.”*

3.1.3 Technology Access

Technology Access 101: Oncode initiated the Technology Access (TA) programme in 2021, which aims to provide the Oncode community with access to emerging technologies that are potentially of high value to Oncode research. The programme will support the assessment of technologies and validate their utility and effectiveness for the Oncode community. The programme supports initial assessment and validation will determine the potential value of the technology for the Oncode community. For those technologies considered sufficiently impactful for the Oncode community, Oncode will either include them in its I&T programme or support the securing of external funds.

A pilot version was initiated in 2021 to test the potential of this programme. A Technology Access Board (TAB) comprising 7 OIs, assessed 14 proposed technologies that could be suitable for consideration in the pilot. Three technologies were selected to receive funding in 2022 and will be tested in at least 3 different labs per technology to ensure usability. These three technologies are:

- Spatial Transcriptomics (lead OI: Jarno Drost, PMC)
- The Phenocycler (co-detection by indexing) imaging machine (lead OI: Anne Rios, PMC)
- CITE-seq (lead OI: Jop Kind, Hubrecht)

3.1.4 Interview Laura Heitman & Jop Kind

The next generation of excellent scientists

The researchers of Oncode Institute are a diverse mix of talented people with different backgrounds and career paths. An essential element of the Oncode community are the junior Oncode Investigators, talented young group leaders who bring new ideas, techniques and vitality to the community. Laura Heitman is a professor of molecular pharmacology at the Leiden Academic Centre for Drug Research (LACDR). Jop Kind is group leader at the Hubrecht Institute and professor by special appointment of Single Cell Epigenomics at the Radboud University Nijmegen. They spoke with us about the importance of the Oncode community and the value it has for young PI's.

How important is an organization like Oncode for young PI's?

Laura Heitman: 'Being part of this community is very important. Our research takes place at the beginning of the drug discovery pipeline, investigating novel concepts, targets and compounds. The majority of Oncode Investigators work further along the pipeline, with preclinical and clinical models. When I joined Oncode in 2019, I found it both exciting and overwhelming'.

Jop Kind: 'Indeed, there is this general community that is great to be part of. I now know what most investigators within the Oncode community do, because we have had the opportunity to discuss our work during the many Oncode meetings. I now know who to contact if I want patient material or if I want to work on colon cancer. That is extremely valuable.'

Laura Heitman: 'That financial flexibility which comes with the 'base funds' is of course also very helpful. We can now spend our funding on cutting edge science for which it is generally hard to get funding due to lack of preliminary data.'

Jop Kind: 'It is the same for us – we work on technical advances and that is tricky because they are at high risk of failure, but the reward is high if they work. And it is difficult to get funding for this. The Oncode base fund makes this work possible and now it's also easier to apply for follow up funding or use the base fund to do experiments and then use that data to apply for a grant. I got an ERC grant for research that was initially funded from my base fund. Similarly, I now received a grant for a collaboration with Oncode Investigator Jan Paul Medema (Amsterdam UMC), where we develop a new method for diagnostics on blood. That is now funded by the Royal Academy.'

What are the challenges for young PIs and does Oncode help in meeting these challenges?

Laura Heitman: 'To me, the main challenge is acquiring funding – and Oncode offers support here not only through the base fund but also by assisting in writing or editing your grant applications with support

from the Valorization Team. Besides this, a big challenge is supervising a group. There are skills you need to develop, for example on how to interact with the different personalities within

your team. When you supervise PhD students – that period of their lives is quite a challenging one. And of course, you have been a PhD student yourself. But it's an individual trajectory, so each PhD student encounters different challenges and personal issues. I think depending on how the group is expanding, you need to find the best way to supervise your group and give them equal attention even when your agenda is occupied. And these are skills to be learned and Oncode offers support with that'.

Jop Kind: 'Building a group is certainly a big challenge. It is about finding your signature research line, but like Laura said, the mentoring is difficult and building a group with people that you think are compatible. You need matching characters, but you don't want one type of character. Dealing with conflict I still think it is the most difficult part of a lab. You need to take firm action, be honest, you need to be outspoken but not judgemental. And that I find very hard. Oncode's mentoring program helped with that and it's very useful that registering for those courses is just a click away. I'm not sure this would be something we'd easily do otherwise. As a young PI you need to develop those skills. And you learn what to do and what not to do'.

Oncode brings a new model in which basic science and collaboration are combined with valorization. How do you relate to this idea or what has it changed for you?

Laura Heitman: 'I have a lot of contact with the Oncode valorization team, and this makes me more aware of the potential of my discoveries. That is also a skill I haven't developed, so I really need experts and it's great that Oncode provides that as well. I noticed that I often consider myself to be too 'basic' or academic and I don't see that the work that we do can be valorized. Someone needs to point me towards that. And while I have access to the valorization team from the university, they need to serve the whole university, their time is limited. The ratio between the number of people in the valorization team within the university versus the university's staff is something to consider. In contrast, I feel that I can more easily reach out to the Oncode team, that they have more time for me and have "on topic" expertise.

Jop Kind: 'It is the same for me. I came to value Oncode's valorization support very much. At first, I was a bit sceptical. I had no experience with valorization except for this annoying paragraph in grant applications, where you have to fill in something. It is hard to fill in when you do basic science. But now I have frequent contact with Veerle Fleskens, my business developer. She does a lot of the thinking for us; she sees opportunities in grants and applying for grants but also for collaborations. An example of something I really want to develop further is a powerful technology allowing for diagnostics based on liquid biopsies in blood. With low volumes of blood, based on the epigenetics of the DNA and the histones - we can tell if a person potentially has a tumour, what type of tumour, and perhaps the grade of the tumour. This is a pilot project I am currently doing with Jan Paul Medema. If successful, we potentially want to build a spin-off company around the technology to be able to further develop it. I never would have imagined starting a spin-off, but thanks to Oncode's Valorization Team, I'm very aware of such possibilities."

Oncode's goal for the upcoming years is to enable the next game changing research in the fight against cancer. What are the game changers you want to address?

Jop Kind: Developing innovative tools and diagnostics which really benefit cancer diagnostics and research. We are now starting to apply the technologies we developed over the years and start implementing them – for example in the collaborations with Jarno Drost, Jacco van Rheenen and Jan Paul Medema. We will be using the basic science that we developed, with the freedom that we had, use that knowledge we gained and start making a difference in cancer research'.

Laura Heitman: I will continue my research on novel concepts for drug discovery, basically trying to find novel chemical modalities to intervene with protein function. One such concept involves protein degradation. A proven concept for many types of enzymes, but not yet for membrane bound enzymes, which is my field of interest. This is a typical high risk research line, requiring both new technical skills and the expertise to synthesize new compounds. Using my base fund, we have made considerable strides forward, all essential 'pieces' are in place, now let's see whether we can degrade membrane proteins as well'.

3.2 Collaboration

Oncode aims to drive innovation through collaboration, fostering a culture of openness and sharing in which researchers can engage in cross-disciplinary collaborations, with different scientific groups, clinicians, and other public and private research organizations. To achieve this objective, Oncode has built collaboration into every aspect of its operations. Firstly, through Oncode's 12 partner institutes are interconnected providing Oncode researchers with a nationwide network of facilities, scientific and clinical experts, together with their research, (patient) data and samples. Secondly, by promoting collaborative research through targeted funding programmes that require joint applications by multiple OIs or applications together with a clinician. Thirdly, by providing its community with multiple platforms for interaction, ranging from large, institute-wide annual meetings and conferences to small-scale focused technical masterclasses and clinical workshops. Lastly, by proactively reaching out to industry to identify opportunities for collaboration via its Industry Engagement (IE) programme. While the ongoing COVID-19 pandemic prevented some of these activities in 2021, Oncode continued to organize meetings both online, face to face, and hybrid to ensure interactions could continue.

3.2.1 Meeting people during the COVID-19 pandemic

Community building 101: Social interactions play a vital role within Oncode's scientific community, allowing constructive discussion, the exchange of new ideas and opinions, the forging of new collaborations, and the strengthening of existing relationships. The COVID-19 pandemic and the resulting social distancing regulations had a major impact on face to face interactions within the Oncode community. Based on the adaptations Oncode put in place in 2020, the first year of the pandemic, Oncode was able to continue

organizing a wide variety of meetings throughout the year. Depending on the restrictions in place at certain times, Oncode shifted easily from fully online to hybrid or face to face meetings. This enabled the community to share research, learn, and engage with its network to bring about new interactions between researchers, clinicians, patients, and industry representatives in new ways.

During 2021, Oncode organized 8 meetings attracting a total of 1250 participants. In addition to Oncode's standard meetings such as its [clinical workshops](#), annual conferences, OI meetings, and technical masterclasses, a new type of meeting was added to Oncode's repertoire in 2021 – namely, the [Postdoc Retreat](#). This two-day event set in the forests near Lunteren brought together 46 postdoctoral researchers from Oncode partner institutes across the Netherlands. The programme included scientific sessions covering a wide variety of topics, two keynote lectures, workshops on Intellectual Property, entrepreneurship, and career development, and most importantly, lots of breaks for informal talks and networking.

Training programme: Oncode believes in the importance of educating and training future generations of researchers. As in previous years, Oncode successfully offered its community a wide range of face-to-face workshops, masterclasses, and mentoring sessions in 2021. Working within the constraints of COVID-related social distancing regulations and lockdowns, Oncode hosted three masterclasses and one workshop in collaboration with OIs, and the I&T programme. In these masterclasses/workshops, experts (Oncode researchers and invited speakers) discussed the latest scientific discoveries and technical developments in their field. In addition, the expertise, technical possibilities, and/or opportunities for hands-on support available to research projects via Oncode's facilities were showcased. Topics such as "[Single-cell genomics/epigenomics](#)" and "[Technologies and model systems used in genome \(in\)stability research](#)" were covered. In total, Oncode organized 5 masterclasses. The workshops and masterclasses were highly appreciated as witnessed by some of the quotes provided by participants:

"To get a general idea of the state of the art and applications of these single-cell technologies, and who to contact in case we need help in experiments."

"It was a great overview of which technologies are used and developed in the Oncode network. Furthermore, it was a great opportunity to talk to the speakers."

"Nice to see very different techniques discussed by experts in the field."

3.2.2 Patient Engagement

Patient Engagement 101: Patients and researchers are inherently linked but rarely meet. In different ways, both patients and researchers have their lives deeply affected by cancer. Getting researchers and patients together is a chance to access first-hand knowledge and improve research through novel ideas, perspectives, and discussions.

Oncode ensures that the patient perspective is well represented within the institute's actions, ranging from patient representation in our chief advisory boards and inclusion of the patient perspective in our communications, to well-defined support structures that enable researchers and [ex-]patients to connect and interact.

Patient Perspective programme: In 2019, Oncode set about establishing a **pilot study** in which (ex)cancer patients and researchers could regularly meet to discuss their experiences. The pilot study was initiated in NKI and LUMC in early 2020, initially with 5 research groups participating. As a result of persistent promotion during **Oncode meetings** and **news items**, the programme steadily gained more and more traction. In 2021, 3 more research groups joined the programme and a total of 11 (ex)patients now informally interact with members of 6 Oncode research groups on a regular basis, while 2 groups are searching for suitable childhood cancer survivors as patient partners.

Sadly, 2021 was also marked by the death due to lung cancer of **Boelien Geerts**, one of the first patient representatives in Oncode's Patient Engagement Programme. Oncode is immensely grateful to Boelien for all her efforts. Her dedication, energy, and positive attitude have inspired many within Oncode and she will remain in our hearts and minds forever.

***Karin de Visser**, (NKI): "Questions from patients can be very different to those from fellow researchers, which may provide new insights into your research."*

***Inge Reus**, (patient partner): "I am looking forward to another session. How wonderful to still be able to learn so much [from patients], because the disease cancer also brings many positive experiences, and I am grateful for that."*

***Marten Hornsveld**, (researcher LUMC): "The fact that pancreatic cancer leads to a lot of stomach pain made me decide to look into co-culturing cells of the nervous system in my pancreatic cancer models."*

***Jacco van Rheenen**, (NKI): "The van Rheenen lab is a multidisciplinary team of biologists, geneticists, biophysicists, and medical doctors. We collaborate with multiple international leaders in a wide variety of fields. In other words, we get input on our research from different perspectives. However, the only perspective that we missed was from patients. By involving patients in our research, we will fill this gap."*

Patient engagement crossing borders: 2021 was marked by Oncode's Patient Engagement programme, which reached out to other (inter-)national institutes and initiatives to collaborate on the topic of patient engagement. Through these outreach activities, Oncode aims to learn from and/or inspire other initiatives that already have experience of patient engagement or have the ambition to engage with patients. The programme has now built ties with multiple initiatives namely:

- In collaboration with **University Utrecht**, Oncode set up an interactive lecture on patient participation for the 'Oog voor impact' course delivered to more than 100 bachelor students in the biomedical sciences. The lecture featured a team of 2 patient partners and 3 Oncode researchers, who shared their experiences within the Oncode Patient Perspective programme.
- A group of clinical and psycho-social researchers working in oncology at **Lausanne University** are currently building a platform to foster public, patient, and caregiver involvement in cancer

research. Eager to learn, they reached out to hear Oncode's experiences on building a patient engagement programme.

- In 2021, Oncode was instrumental in setting up a pan-European research initiative. In late 2021, the European Commission (EC) launched a one-year Coordination and Supportive Action called ***Understanding Cancer (UNCAN).eu*** with the goal to generate a blueprint for the UNCAN.eu virtual institute. The blueprint will be organized as a research roadmap, focused on a limited number of challenges within cancer research, prevention, and treatment that urgently need to be addressed. Oncode expects to become actively engaged in the setting up of multiple scientific work packages. Importantly, Oncode's Patient Engagement programme will participate in a work package titled 'Patients and European Citizens in Cancer Research'. This work package aims to engage and empower patients and European citizens in UNCAN projects and ensure that UNCAN takes patients' unmet needs and priorities into consideration in each work package. If funding is awarded, the lessons learned in Oncode's unique patient engagement programme could potentially be rolled out on a much larger scale.

Student University Utrecht: "I have learned today that you have to involve patients in every step of cancer research. It is very rewarding for both patients and researchers in all types of research, not only in for example, clinical trials."

3.2.3 Public Private Partnerships

Public Private Partnerships 101: Oncode aims to enable the efficient translation of Oncode research findings into better treatments and diagnostics for cancer patients. To do so, it promotes interdisciplinary collaboration with industrial partners, continuously investing in building long-lasting relationships and identifying opportunities for collaboration with industry. Through the day-to-day actions of Oncode's valorization team and its proactive Industry Engagement programme, Oncode has built an extensive (inter)national network of industry partners to facilitate public private collaborations. This network can be readily accessed by Oncode business developers when opportunities for collaboration arise. Oncode's expertise in arranging legal and financial frameworks for Public Private Partnerships (PPP) helps to accelerate the set-up and execution of these collaborations.

Oncode is currently in contact with 93% of the oncology-related SMEs in The Netherlands. The large majority of OIs are now collaborating with or in discussion with industry. Moreover, the total contract value with industry has increased more than 14 times since the initiation of Oncode, from €1.3M in 2018 to €18.7M in 2021. Furthermore, in 2021 Oncode business developers brokered 249 new agreements with industry ranging from confidentiality disclosure agreements (CDAs) and collaborative research agreements to license agreements.

Alexander van Oudenaarden (Hubrecht Institute): "Oncode facilitates collaborations and contact with companies. In the last year we were contacted by several companies and Oncode really helps streamlining these interactions by making sure all paperwork is in order and agreements are clear."

Leila Akkari (NKI): "In search for companies interested in targeting myeloid cells in challenging cancers like glioblastoma, Oncode put me in touch with a relatively young but very dynamic company called Iteos, which is run by scientists still very close to the bench, like us. Without my business developer Yuva Oz identifying this company and knowing it would fit my expectations and needs, I would not have reached out to them."

A PPP in the spotlight: "I have been intrigued by how one single factor could elicit so many different biological effects ever since I was a master's student", says OI [Peter ten Dijke](#) (LUMC). He means the TGF- β growth factor, to which he eventually devoted his entire career. It was by chance that during a scientific conference, Peter came across antibody of interest of a well-established biopharma company. The antibody targets a highly conserved bone morphogenetic protein antagonist and a member of the Transforming Growth Factor- β superfamily, a pathway which Peter is all too familiar with. Following a fruitful discussion, Peter saw the potential for a collaboration and informed the Oncode valorization team. Oncode business developer Yuva Oz set-up a meeting between the company's scientists, Peter ten Dijke's team, and Oncode to discuss whether it might be of interest to investigate if inhibition of the target of interest with the company's antibody might be synergistic with immunotherapy. A public-private partnership was in the making.

Yuva Oz instantly recognized that the *in-vivo* mouse work in the project could benefit from the expertise of Jos Jonkers' lab at NKI. As it turned out, the addition of postdoc Julie Houthuijzen from the Jonkers lab turned out to be the missing link for the project. The team quickly changed gear, with Peter and Julie writing the project plan and the Oncode BD team setting up a collaborative research proposal and agreement. Oncode led the negotiations for the project plan and the agreement between both institutes and secured an 18-month, ~€360K project with exciting scientific elements spanning NKI and LUMC.

A crisis calls for collaboration across the field: The SARS-CoV-2 pandemic placed unprecedented pressure on diagnostic systems worldwide. At the start of the pandemic, the Netherlands was completely unprepared to carry out the massive testing needed to monitor and control the spread of the virus. OIs Marvin Tanenbaum and Wouter de Laat (both from the Hubrecht Institute) wanted to contribute their scientific knowledge and expertise to combat the impact of the virus and brought together a large group of researchers at the Hubrecht Institute. In early 2020, they came up with a new, fast, and cost-effective method for diagnosing COVID-19. The validation and large-scale implementation of this new method called for a collaborative initiative involving academia, industry, and government. Scientists from the biotech company [Genmab](#) and a regional COVID-19 center – the [Laboratory for Pathology and Medical Microbiology \(PAMM\)](#) – were quickly contacted, resulting in the birth of the 'Systematic Testing using Robotics and Innovation during Pandemics' (STRIP) consortium. The consortium developed and implemented a test robot (lovingly called 'the Beast') with the capacity to make PCR testing possible on a much larger and more cost-effective scale. Oncode quickly recognized the potential and supported this extraordinary public-private partnership by prefinancing the purchase of the required robotics platform. In January 2021, the Dutch Minister of Health Hugo de Jonge [officially launched](#) the newly installed STRIP-1 test robot at the PAMM laboratories. Currently, the Dutch government has installed five additional STRIP robots to use during the current pandemic, which could also be deployed during future pandemics. In a

recent [Nature Biotechnology](#) paper, the test protocol as well as the history of this extraordinary consortium was published.

Hugo de Jonge (Dutch Minister of Health): “The STRIP can be an important additional link in large-scale testing, which is necessary in a pandemic. It is wonderful that companies and institutes in The Netherlands have managed to do this, and the government has been happy to cooperate.”

Rallying the sector: Oncode-PACT: Through the ‘National Growth Fund’, the Dutch government will invest up to €20 billion in projects within the areas of either 1) knowledge development, or 2) research, development, and innovation, to create structural and sustainable economic growth. When the ministry of Economic Affairs announced the second call for projects in early 2021, Oncode was quick to respond and rally the sector to propose a unique project called Oncode-PACT (Preclinical Accelerator for Cancer Treatments), which was submitted in November 2021.

The goal of Oncode-PACT is to bring together the best academic researchers and biotech companies and build a state-of-the-art drug development infrastructure that will not only be easily accessible but also able to innovate the drug development process itself. Oncode-PACT will build early validation and de-risking into the drug development pipeline, ultimately increasing the chances of bringing new therapies to patients.

The project will combine all the expertise needed for cancer drug development into one accessible pipeline and innovate the drug development process via more relevant research models and detailed clinical data from well-defined patient populations. Based on the existing infrastructure that Oncode Institute and the PACT-partners have built up, Oncode-PACT aims to place the Netherlands at the heart of international efforts in oncological drug development. The effect this will have on Dutch biotech and pharmaceutical companies is expected to generate lasting economic impact. The platform will be accessible to any academic institution or company in the Netherlands.

More than forty leading parties from the oncology ecosystem have already joined the consortium to implement Oncode-PACT, including SMEs, large companies, universities, UMCs, research institutes, and social partners. Oncode is proud of the proposal and is confident it will be funded. Oncode-PACT and its many partners will create positive long-term social and economic impact in the Netherlands. By the end of April 2022, it will be clear if the proposal will be approved for funding.

3.2.4 Oncode Accelerator Projects

Since its start, Oncode has invested in building an interactive research community in the strong belief that the establishment of interactions between scientists across different disciplines and expertise can act as the driving force for new research questions and approaches. In late 2020, Oncode launched a new class of projects called Oncode Accelerator Projects (OAPs). Through OAPs, Oncode seeks to increase synergy not only by bringing OIs together in a single project, but also by uniting OIs with non-Oncode researchers, clinicians, and industry to form multi-disciplinary teams that can address unmet medical needs or

scientific challenges identified by the Oncode community through innovative high risk, high reward approaches.

Oncode launched a call for OAP suggestions and 23 project ideas were submitted by different teams of OIs. These were subsequently presented and discussed with fellow OIs in multiple sessions. Of the submitted projects, five were invited to submit a full project proposal for review by Oncode's International Advisory Board. Three projects were eventually chosen for inclusion in Oncode's phase 2 strategy. Because Oncode is currently unable to fund these OAPs through its phase 2 core funding, the projects will be required to attract alternative sources of funding. To date, two projects have already attracted funding from external partners and Oncode anticipates that funding from alternatives sources to support the third OAP in phase 2 will be secured. For the two funded OAPs:

- A team of 8 research groups from 5 partner institutes and an industry partner will be led by OI Bas van Steensel (NKI), who has attracted €4.4M of private funding for a project entitled: Finding regulatory mutations in the non-coding cancer genome (see interview with Bas van Steensel).
- A team of 11 research groups from 6 partner institutes led by OI Sjoerd van der Burg (LUMC) has attracted €3.4M from KWF for a project entitled: Curing tumours difficult to treat with immunotherapy by mobilizing innate leukocytes. Participating research groups will collectively add €1.6M to the KWF contribution.

The OAPs will form a new central element in Oncode's phase 2 strategy, and it is expected that new calls for project ideas will be initiated in future as the phase 2 budget becomes clearer.

3.2.4 Interview with Bas van Steensel

From networking dinners to matchmaking events: how Oncode fosters interdisciplinary collaboration

One of the goals of Oncode Institute is to enable interdisciplinary research collaborations. To this end, Oncode launched a new initiative called 'Oncode Accelerator Projects' (OAPs) in 2021. The goal of OAPs is to form a multidisciplinary team that can uniquely address an unmet medical need or scientific challenge through innovative high risk-high reward approaches. The OAP initiated by Oncode Investigator Bas van Steensel of the Netherlands Cancer Institute is an inspiring example of the fruitful interdisciplinary collaboration that this may yield.

What is this Oncode Accelerator Project about?

"The idea for this project had been simmering for quite some time already. My research group had studied the association between genomic variants and gene expression at the population level. As you probably know, the genome of one person displays millions of tiny differences from the genome of another person.

These differences are called ‘genomic variants’. When located in the protein-coding parts of the DNA, genomic variants may be associated with phenotypic variation such as ABO blood type or genetic disorders such as Huntington disease. However, around 97% of genomic variants are located in the non-coding parts of our DNA. It is much more difficult to interpret these variants. The non-coding DNA is the realm of the enhancers, promoters, and silencers that regulate gene expression, but it also contains large segments that do not appear to have any function. Hence, it is hard to tell whether non-coding variants have functional effects. My lab has developed a technology to assess this at the level of complete genomes.”

“At an Oncode meeting, I spontaneously got talking to Michiel Vermeulen of Radboud University. His group is specialized in studying the mechanistic aspects of how transcription factors bind to regulatory elements of the genome. These are molecular biological studies in biochemical assays. Our approaches nicely complement each other, so we started to collaborate. This quickly went off and we managed to publish our results in a nice journal in 2019.”

What is the link with cancer research?

“Cells acquire tens of thousands of mutations on the journey from healthy cell to pre-tumour cell to tumour cell. When located in coding DNA, it is relatively easy to establish the functional effects of these mutations. It is much more difficult to interpret the non-coding mutations. Mapping the association of these DNA variants with gene expression may greatly increase our insight into their role in the disease process. Enter the third group on our running train: the group of Lude Franke at UMCG. Lude is a geneticist and a renowned expert in bioinformatics. His group had already helped us with the analysis of our previous data. The three of us realized that our complementary tools and expertise would enable us to assess the functional effects of non-coding variants in genomes of cancer cells. Next, I talked with Sarah Derks of VUmc at an Oncode dinner. She is a physician scientist that works on gastroesophageal cancer. This type of cancer often cannot be explained by coding variants, so her group was a natural addition to our team, and they became the fourth partner.”

How did you move from this early research idea to a mature research project?

“In 2021, Oncode launched a call for Oncode Accelerator Projects. This call was not associated with funding, but rather aimed to bring together scientists across different disciplines and fields of expertise. Oncode organized a brainstorm session, where Oncode Investigators pitched their research ideas. At this event, we explicitly searched for natural partners that would further complement the expertise of our team. The groups of Emile Voest, Jeroen de Ridder, and Wilbert Zwart joined us, each bringing unique complementary expertise. After consulting Hugo Snippert and others, we wrote an exciting project proposal, aiming to investigate non-coding variants in tumour cell genomes of patients with gastric or intestinal cancer. In the short term, we would like to unravel which non-coding variants in these cancer genomes have regulatory effects and establish the nature of these effects. Ultimately, this may provide crucial information that clinicians can use to select the most promising therapy for individual patients. Our dream is to develop an algorithm that interprets tumour sequencing data and flags points of attention for clinicians. This may be feasible within ten years or so.”

“We managed to attract external funding through the Antoni van Leeuwenhoek Foundation, and the project kicked off in Fall 2021. The first datasets have been generated, and together with the Zwart Group – who are experts in genomics analysis of tumour samples – we are ramping up these efforts. Our unique technology produces immensely large datasets, with millions of measurements. The groups of De Ridder and Franke lead the bioinformatics analysis of the data, and the Vermeulen Group will perform the mechanistic interpretation. The Voest and Derks Groups bring in their view on what matters to patients. In addition, they are experts in using organoids and clinical materials to verify the results of the computational models. So, our groups really form a natural match rather than the type of forced collaboration that you often see in consortia.”

What is your view on collaboration in general?

In my opinion, it is absurd if cancer researchers compete. This is not what public research money is meant for. Therefore, I actively contact peer researchers if I discover that they are working on overlapping topics, so that we can coordinate our efforts, collaborate, and exchange expertise. My lab also runs an Open Science Blog, where we try to inform people of ongoing work. We hope that this contributes to a more productive, collaborative, open kind of science. Collaboration is a strong means to realize goals and it can be a lot of fun. However, collaborations do call for investments of energy and time, as well as good communication and clear agreements. So, I try to choose my research partners wisely and search for those that are truly complementary as well as committed. Being part of Oncode forges a bond between different labs across the country, promoting this type of commitment.”

3.3 Valorization

Oncode has developed an overarching valorization strategy to speed up the translation of new insights in cancer biology into tangible applications for patients, society, and the oncology community. Key to Oncode’s valorization strategy are its affiliation agreements with Partner Institutes, which grant Oncode the exclusive right to manage and commercialize the intellectual property (IP) rights developed by an OI and his/her lab. This effectively means that over 900 Oncode researchers work together to execute a single strategy focused on oncology and receive proactive support to bring their discoveries/inventions to patients and society. A substantial fraction of Oncode funding (~16% for the first 5-year phase) is dedicated to the actions of the valorization team, an international team of 7 business developers, 1 fund manager, a valorization coordinator, and a data entry operator. The valorization team is the first point of contact for OIs and their research groups. As a result, Oncode’s business developers have become an integrated part of the research groups, which has the benefit that inventions are recognized earlier so that suitable valorization channels can be identified and activated swiftly. Furthermore, the availability of dedicated valorization funds enables Oncode business developers to swiftly adapt proposals and act on new opportunities. In 2021, the valorization team was very active and, as it did in 2020, surpassed the yearly targets set at the outset of Oncode. See figures below.

3.3.1 Impact of Technology Development fund

Technology development fund 101: The Oncode Technology Development Fund (TechDev fund) was established to address scientific, technical, and business issues with the aim of increasing the likelihood that Oncode inventions can be licensed and further developed. The fund is managed by the Valorization Team and all projects are directly associated with an Oncode invention. Projects include activities such as drug target validation, high throughput screening, medicinal chemistry, toxicological studies, pK/pD studies, the formulation of drugs to support Oncode CPoC clinical trials, and health technology assessments (HTAs). With a total budget of €4M, the fund has so far funded 24 projects of which 7 were awarded in 2021. Six projects were completed in 2021. The value of the TechDev fund is particularly well illustrated by the two examples below.

Carl Figdor (Radboud UMC) - €149K, 1.5 years: Dr Carl Figdor (Radboud UMC) is a renowned expert in the field of tumour immunology. His research group aims to understand the function of antigen presenting cells (APCs) as major regulators of immune response and harness their function for the development of cancer immunotherapies. Adoptive cell treatments, such as TIL or CAR-T- therapy, require T-cells from the patient to be removed, engineered ex-vivo and re-infused into the patient in order to stimulate the immune system to recognize tumour cells. While this has emerged as a powerful and potentially curative therapy for certain cancers (two CAR-T therapies entered the market after FDA approval in 2017), the approach suffers from issues. For example, it was only effective in a subset of patients, and it is an autologous therapy that has therapy-associated toxicity and high production and administrative costs. The Figdor lab at RUMC has created a modular, polymer-based, off-the-shelf antigen presenting cell that can be loaded with key signalling molecules to stimulate the immune system to generate immune cells primed against antigens of choice.

While this novel technology can be used ex-vivo as the T cell activating agent in CAR-T therapy, its real novelty lies in its ability to be administered in-vivo, eliminating the need for ex-vivo manipulation. Through Oncode's TechDev Fund support, the Figdor lab was able to generate in-vivo proof of concept, which supported the launch of Oncode's 7th spin-off company ([Simmunext biotherapeutics](#)) in March 2022. The company will develop a technology platform for both ex-vivo and in-vivo activation of a wide variety of tumour-reactive T cells, such as B-cells, NK cells, TILs and DCs in the fields of oncology, (auto)immune, and infectious disease.

***Carl Figdor:** "The Tech Dev grant has been very important for performing the experiments needed to turn our findings into a product. With its support in getting the Tech Dev grant, Oncode expedited the in vivo experiments in mice, and by that - supported me in taking the first steps towards translation into the clinic".*

Rebecca Schneider (EMC) - €95K, 1.5 years: To date, there are no effective therapy options for patients suffering from myeloproliferative neoplasms (MPNs), a rare blood cancer in which patients' bone marrow produces excess platelets and red and white blood cells. Furthermore, no therapy is in development or has been evaluated in the clinic that clearly demonstrates the ability to target the disease-causing mutated hematopoietic stem cells. Work from the Schneider lab has shown that bone marrow stromal cells can act as protagonists of the mechanisms underlying this blood cancer type and might therefore provide a long-sought therapeutic target.

In a CPoC study (see section 3.3.2) the Schneider group is investigating the effects of a new type of small molecule drug which acts on the bone marrow stromal cells and could therefore be relevant for patients suffering from MPNs. Work in the Schneider lab has provided indications that multiple molecular pathways underlie MPNs, and pharmacologic interference in these intertwined molecular mechanisms could potentially lead to a more pronounced effect on disease progression. Within this TechDev project, Dr. Schneider will evaluate if the effects of standard-of-care treatment for MPNs can be increased when combined with this new therapy, which is currently being tested in a phase 3 clinical trials for prostate cancer. The TechDev project will be used to gain the additional data needed to gain a more solid IP position for the use of a small molecule inhibitor alongside existing therapies. Through negotiation with the industry partner currently developing the new therapy, Oncode has ensured the compound is available for use in the TechDev and CPoC projects.

3.3.2 Achieving Proof of Concept

Clinical proof of concept 101: Oncode aims to accelerate the translation of academic research findings into better diagnostics and better treatments for cancer patients. To that end, it focuses on de-risking innovations at an early stage. Oncode has a dedicated fund (total €10M) to invest in (pre)clinical proof-of-concept studies to demonstrate the potential diagnostic or therapeutic value of a research finding. Oncode's team of experts provides guidance and advice to all OIs applying for Clinical Proof-of-Concept (CPoC) funding. In 2021, Oncode awarded 4 CPoC projects with a total budget of €2.8M. Out of a total of 17 awarded CPoC projects awarded by Oncode up to the end of 2021, 3 have now been completed.

To increase interaction between basic scientists and clinicians, Oncode organizes clinical workshops that aim to facilitate a dialogue about clinical challenges and how scientific insights can contribute to solving them. Due to the impact of the COVID-19 pandemic, Oncode was only able to host one of these **clinical workshops** in 2021, centered around melanoma. Clinician Karijn Suijkerbuijk (UMCU) and OI Sjoerd van der Burg (LUMC) hosted the workshop, which brought together 44 experts with different fields of expertise from across the Netherlands.

New project in the spotlight: Oncode is pleased that the flow of high-quality projects continues to make its way towards the clinic. In 2021, projects were awarded to Edwin Cuppen (UMC Utrecht, see below),

Maarten van Lohuizen (NKI) , Rebekka Schneider (Erasmus MC) and Sjoerd van der Burg (LUMC), the last three listed being in collaboration with industry partners.

GLOW study: In 2019, Edwin Cuppen attended a clinical workshop organized by Oncode focused on glioblastoma. Recognizing the unmet clinical need for more effective treatment strategies, Cuppen quickly recognized the potential of whole genome sequencing (WGS) in helping to combat this disease. Cuppen contacted multiple clinicians to discuss the issue and eventually set up a CPoC project. The project team submitted the 'GLOW' (Glioblastoma targeted treatment option maximisation by WGS) study proposal, in which Cuppen together with clinicians Filip de Vos (UMC Utrecht) and Marike Broekman (Haaglanden MC) will investigate the added value of WGS on tumour tissue obtained from glioblastoma patients during routine operations for a first relapse after standard treatment with chemo and radiotherapy. The goal of the GLOW project is to find suitable treatments with targeted medication as well as additional treatment options. [Funding for the project was awarded in May 2021.](#)

Glioblastomas are the most common malignant primary brain tumours, affecting approximately 1,000 patients per year in the Netherlands. The prognosis for these patients is very unfavourable, with only ~17% of patients still alive after two years. Despite extensive research into the biology of these tumours, the standard of care has hardly changed over the past 15 years. New treatment strategies are therefore urgently needed. The aim of this project is not only to provide additional therapeutic options for patients with recurrent glioblastomas, but also to contribute new insights into the biology of these deadly tumours. The project therefore has the potential to change the standard of care for patients with glioblastoma.

Filip de Vos, MD (UMC Utrecht): "The unmet clinical need of discovering new treatments is almost palpable in operating and consulting rooms when we treat glioblastoma patients. GLOW presents a unique opportunity to examine the promise of whole genome sequencing in delivering accurate personalized treatment as an addition to expert neuro-oncology care in major Dutch centers."

Edwin Cuppen (UMC Utrecht): "Following the Oncode glioblastoma workshop in Rotterdam, I started working with a number of clinicians to develop a clinical proof-of-concept study."

First 'Oncode' therapeutic tested in patients: In 2019, Oncode awarded a grant to OI Sjoerd van der Burg, his colleague Thorbald van Hall (both LUMC), and pulmonary oncologist Joachim Aerts (Erasmus MC) to develop a potential anticancer vaccine called TEIPP (T-cell epitopes associated with impaired peptide processing) targeting immunotherapy. The project consisted of preclinical validation work, which if successful would be followed by a clinical trial. In 2021, Oncode was proud to announce that a clinical trial with the project's newly developed vaccine against Non-Small Cell Lung Cancer (NSCLC) started at Erasmus MC.

The newly developed vaccine, which teaches the immune system of lung cancer patients to recognize and clear their own tumour cells, could offer relief to a large proportion of nearly 10,000 patients who receive a NSCLC diagnosis each year in the Netherlands. NSCLC is the most common form of lung cancer and in

80% of cases is unresponsive to existing treatments, including immunotherapy, at the time of diagnosis. Treatment options for these patients are therefore very limited. The research team led by Sjoerd van der Burg hopes to change this with an innovative approach based on a therapeutic vaccine. The phase 1/2 clinical trial launched in November 2021 will look at the safety and tolerability of the vaccine and the dose needed to elicit a good immune response in 24 patients, with the first results expected in 2023.

Oncode is particularly proud of this new milestone. Since its foundation in 2018, the institute has focused on funding fundamental cancer research and translating its results into practical applications for patients. Oncode offers various funding opportunities to accelerate this translation. The vaccine that will be tested is a new product. Oncode recognized the potential of the basic research finding early on and was able to utilize its TechDev fund to enable quick maturation of the technology, which was promptly followed by the CPoC grant.

Chris de Jonghe (Oncode) "It took only three years from the first publication of the research results to the start of this clinical trial. This underlines Oncode's mission to accelerate the translation of fundamental research into new treatments for patients. And of course, we hope for positive outcomes for patients with lung cancer."

3.3.3 Oncode Oncology Bridge Fund

Bridge fund 101: The Oncode Oncology Bridge Fund, managed by Oncode B.V., is an investment fund of €7.2M that provides pre-seed and seed capital to commercially viable enterprises originating from within the Oncode community to help translate their research ideas into market-ready investment opportunities. This can include new therapeutic interventions, diagnostic screening tools and services, biomarkers, research tools or services that will benefit either cancer patients or cancer research in general. Early-stage investments are accompanied by professional intellectual property management, follow-on financing, technology de-risking, and where possible, preliminary clinical validation. Additionally, the Oncology Bridge Fund prepares new enterprises for follow-on investments from private investors such as 'angels' or venture capitalists. Oncode B.V. has committed €1.1M of investment capital in 7 spin-off companies, which currently employ 17 FTEs. In addition, 8 Oncode projects (or technology opportunities) are in the ideation/validation stage prior to possibly launching as spin-off companies. In 2021, the Oncology Bridge Fund committed €600K of investment capital in 2 spin-off companies.

Checking back with Immagine: Last year, Oncode and the NKI proudly launched Oncode's 5th spin-off; **Immagine B.V.** Originating from the lab of OI Prof. Daniel Peeper and Prof. Christian Blank (both NKI), the company is focused on developing next-generation precision immuno-oncology (IO) treatments. In 2021, the spin-off announced it had successfully raised seed financing to advance its next generation IO therapeutics. BOM Brabant Ventures joined as a new investor with additional support from existing investors Swanbridge Capital and Oncode Oncology Bridge Fund. The company will use the new funding to further develop its proprietary pipeline of targeted immunotherapies for cancer patients utilizing its

Immunogram approach. This approach identifies limitations of state-of-the-art cancer immunotherapies, and uses guided target identification and patient stratification to enhance therapeutic outcomes.

The Immagine enterprise grew with the appointment of Jac Wijkmans, who brings extensive drug development experience, as Chief Scientific Officer. Under his leadership, multiple drug candidates have been optimized and selected for pre-clinical and clinical studies.

***Dr. Maarten Ligtenberg** (CEO Immagine): “I am excited that this syndicate of investors has come together to support the further development of our IO programs, and I’d like to welcome BOM Ventures as investor. I am especially pleased that industry veteran and experienced R&D executive Jac Wijkmans will be joining our team as CSO to direct our drug development endeavours.”*

***Mercedes Tuin** (Investment Manager at BOM): “Immagine’s platform-based target selection has shown the potential to identify novel targets for which it is developing new small molecules for effective immunotherapy in cancer. This approach fits well with our focus and the strength of the local ecosystem in IO and precision medicine. We are excited to work with the team to advance their ground-breaking therapies.”*

Oncode and NKI’s second spin out: Following the launch of Immagine from the NKI in 2020, Oncode and the NKI launched their second joint spin out - Oncosence - in 2021, a company building on 5 years of research from Ol René Bernards, who focuses on understanding senescence and its role in tumour biology.

The company is based on breakthrough findings from the Bernards lab, showing that certain types of cancer can be treated with what is called ‘the one-two punch’ approach. In a 2019 Nature publication, Bernards showed that senescence can be induced by one drug, followed by a second drug to kill the senescent cancer cells. The launch of Oncosence coincided with the onboarding of a management team that will execute ideas to develop this therapeutic combination efficiently and at pace. With targets already identified and validated, and an initial investment from the Oncode Bridge Fund, the company is now gearing up to raise additional funds to develop the targets clinically.

***René Bernards** (NKI): “What makes Oncosence unique is that we are trying a completely new approach to the treatment of cancer that relates to the induction of senescence for cancer therapy. Until now this has never been done.”*

Oncode’s latest spin-off: In 2021, Oncode Institute and ArgoBio teamed up with Ol Madelon Maurice at UMC Utrecht to launch Laigo Bio, a new company in the emerging field of target protein degradation. Both the Oncode Bridge Fund and ArgoBio invested funds to further develop Laigo Bio’s proprietary pipeline of SureTACsR targeted immunotherapies.

Prof. Maurice had already discussed the potential of the technology with Oncode business developer Emil Pot in 2019. Quickly recognizing the potential, Oncode secured the IP using its IP-fund. Prof. Maurice subsequently applied for TechDev funding, enabling her to obtain Proof-of-Concept (PoC) for the technology platform. In the meantime, Oncode and French ‘start up studio’ ArgoBio had been discussing the potential of working more closely together to support and fund innovative early-stage projects. The

SureTACsR technology of Prof. Maurice fitted perfectly with the ambitions of both the Oncode Bridge Fund and ArgoBio.

The SureTACsR technology platform is a novel membrane protein degradation approach applicable to a broad scope of disease applications. The primary focus for applications lies in oncology but the technology has the potential to be applied in parallel programmes in neuro-inflammation and neuro-degenerative diseases. In contrast to other small molecule approaches, the platform results in an efficient and sustained degradation of target receptors, potentially resulting in clinical efficacy superior to the modalities currently being employed by other emerging protein degradation technologies.

Initially driven by Madelon Maurice, who will join as Principal Investigator, Laigo Bio is gearing up for preclinical lead development in the coming months, generating proprietary biologics for a selection of targets to showcase the technology's potential. Laigo Bio receives strong support from seasoned entrepreneurs Neill Moray Mackenzie at ArgoBio and Emil Pot at Oncode, who will prepare the company for a Series A investment round to initiate first clinical studies in 2025.

Dr. Neill Moray Mackenzie (ArgoBio): "This is exactly why we put ArgoBio together last year – to fund these early-stage opportunities. I am especially pleased that Madelon Maurice, a renowned key opinion leader in the field, is leading this novel approach to protein degradation which has great potential to open up a completely new biology in the field of cancer therapy."

Managing the Oncode Oncology Bridge Fund: Since its inception in 2019, the Oncode Oncology Bridge Fund (OBF) has been managed by fund manager Shobhit Dhawan. Dhawan brings with him broad experience in business development and investment management. Since its launch, the fund has made investments in 7 companies, with a full pipeline of new investments expected in the coming years. While the OBF is expected to run until 2025, Dhawan and Oncode Valorization Director Chris De Jonghe are already drawing up the plans for a follow-up fund OBF-2. With Oncode's growing ambitions and expanding pipeline of potential spin-offs, Dhawan and De Jonghe envisage that the OBF-2 fund will be larger, with contributions from Oncode's 'core' public funding plus matching funds from private and/or international public partners. In 2021, the Oncode communication team sat down with Dhawan to talk about the art and challenges of linking researchers, investors, and industry to turn exciting research projects into successful companies. (You can find the full interview [here](#)).

3.3.4 Oncode Strategic funding support

Strategic funding support 101: Oncode's Strategic Funding Support programme aims to help OIs navigate the funding landscape and thereby boost Oncode research funding. The programme provides tailored funding strategies for OIs and spin-off companies, offers training workshops and 'tips & tricks' for acquiring the most frequent types of grant, and collaborates with external parties and funding bodies on training and workshops. In previous years, Oncode business developers proactively engaged with OIs to provide funding support. In 2021, Oncode revised this strategy to create a more balanced utilization of resources, choosing to focus its attention on support through grant reviews and through the provision of (outsourced) support

for strategic projects. Using this amended strategy, the programme successfully met its objectives for 2021 - adjusting resource investment to optimally utilize capacity while maintaining the quality of support. In 2021, the programme achieved a success rate of 52% (compared to 35% last year), and secured total funding of €17.4M, of which €8.6M was allocated to Oncode Institute and Investigators. Upon request, Oncode also provides support to non-Oncode researchers. A typical example is Trudy Straetemans (UMCU), for whom Oncode successfully supported an application for a KWF 'DARE-NL infrastructure for ATMPs' grant of €5.4M.

Other notably successful grants for which the programme provided support include:

- NWO-Vidi grants (€800K) - Hugo Snippert (UMC Utrecht) and Jarno Drost (PMC)
- NWO-Vici grant (€1.5M) – Michiel Vermeulen (Radboud University)
- ERC Starting grant (€1.5M) – Julie Nonnekens (Roland Kanaar group, Erasmus MC)
- KWF Young Investigator grant (€615K) - Florijn Dekkers (Anne Rios group, PMC)

3.3.5 Affordable Health Care programme

Affordable Health Care (AHC) 101: Oncode is dedicated to contributing to the affordability and sustainability of cancer healthcare solutions and aims to do so by leveraging its expertise and position in the valorization value chain to ensure affordability and sustainability obligations are included in applicable Oncode activities. Oncode therefore focuses a significant part of its strategy on this goal. Oncode's activities in relation to AHC are accommodated in many different ways, including education and awareness, funds and programmes aimed at funding research that focuses on reducing the cost of care, health technology assessments, and socially responsible licencing policies.

In addition to its activities in this area, Oncode's communication team also discussed the affordability of health care in general with Henk Verheul (Clinical Oncologist at Radboud UMC and Chair of the Oncode Clinical Advisory Board) and Sipko Mulder (Dutch Ministry of Health member of the management team on pharmaceutical products and medical technology). You can find the interview [here](#).

Investing in clinical proof-of-concept to contribute to affordable health care: Oncode has set itself the objective to ensure that 20% of the clinical activities within its CPoC programme are focused either on personalized medicine (patient stratification) or drug repurposing. An analysis of Oncode's clinical portfolio in 2021 showed that over 58% of clinical projects contribute to AHC. More specifically, 47% of CPoC projects investigate patient stratification and 29% drug repurposing. Below are two examples of how Oncode's CPoC programme is contributing to AHC.

BASALT study (JP. Medema, Amsterdam UMC): In partnership with ZonMw, Oncode has invested in 3 CPoC projects dedicated to AHC (pre)clinical research with a total budget of €~1.5M. One of these studies, titled 'Blood-borne assessments of stromal activation to guide therapy in esophageal adenocarcinoma (BASALT)' and awarded funding of €594K over three years, started in 2021. The study was initiated by OI Jan Paul Medema (Amsterdam UMC) in collaboration with clinician Hanneke van Laarhoven (Amsterdam UMC) and

aims to study the safety and efficacy of a new combination therapy and validate a biomarker for esophageal adenocarcinoma - a type of cancer with poor prognosis (median survival just over 3.5 years). A positive outcome from this study will provide a new treatment regimen and a much-needed stratification tool that have the potential to improve the outcome of currently available therapies.

HDAC inhibitor Vorinostat in resistant BRAF V600 mutated advanced melanoma (Rene Bernards, NKI):

Patients with advanced BRAF V600 mutated (BRAFM) melanoma develop resistance to BRAF inhibitors (BRAFi) and/or MEK inhibitors (MEKi) 6 to 14 months after beginning treatment. This is often associated with secondary mutations in the MAPK pathway (for example, NRAS/KRAS), leading to reactivation of the pathway. Preclinical studies in cell lines and mice have shown that treatment of BRAFi-resistant BRAFM melanoma with Vorinostat leads to selective cell death of BRAF inhibitor resistant cells only, and to a remarkable reduction of tumour volume. Bernards, together with clinician Sophie Wilgenhof (NKI-AVL), has worked on this clinical Proof-of-Concept trial in patients with advanced BRAF V600 mutated melanoma who developed resistance to BRAF inhibitors and/or MEK inhibitors. For this patient group no rational treatment is currently available. Within the study, which included 18 patients, ctDNA was used as a biomarker to detect emerging clones resistant to BRAF inhibitors so that patients could be switched to a short-term purging treatment with Vorinostat before BRAF-MEK inhibition was reintroduced. This short-term treatment with Vorinostat has led to promising results. If this new therapy proves to be potentially useful, the study will be completed using external funding. A follow-up phase 2 clinical study is expected, with the aim of providing clear improvements to the current standard of care. Oncode supported this project by analyzing its potential cost-effectiveness in an early-stage Health Technology Assessment (HTA). This HTA suggested that the addition of Vorinostat may be a cost-effective intervention, via a shorter treatment cycle. Further research will focus on the clinical effectiveness of Vorinostat in combination with BRAF/MEK inhibition, the feasibility to detect resistance in an early phase, and survival and quality of life compared to the current standard of care.

Providing the tools and expertise to enable drug repurposing research: Drug repurposing is an effective approach to rapidly identify novel indications for known drugs and compounds. To support researchers in bringing novel therapeutic applications to patients at affordable cost, Oncode has acquired a next-generation Drug Repurposing Library containing ~6,000 candidate drugs in various stages of clinical development (abandoned, off-patent, launched, etc.). To enable all Oncode researchers to access the library, Oncode has set up the Drug Repurposing programme. This programme funds drug repurposing compound screens and provides the technical infrastructure and expertise required to perform the screens. In addition, copies of the library are provided to both Oncode and non-Oncode researchers who have the means and expertise to perform the screens themselves. The programme was initiated in late 2019, and since then a total of 14 screening programmes from OIs have been approved, of which 6 were undertaken in 2021. Two centres within Leiden UMC and NKI have unique drug screening expertise and are able to provide researchers with tailored guidance and support as well as access to a multitude of different assays. Read about the experiences of OI Roland Kanaar with the NKI's centre of expertise [here](#). The library has also been provided to 3 non-Oncode research projects, one of which was aimed at finding therapeutic solutions to COVID-19. Below are two success stories of the Oncode Drug Repurposing programme:

Repurposed drugs enter the fight against breast cancer: Estrogen receptor (ER) is considered the main driver in ~70% of all breast cancer cases, and multiple therapeutic options have been developed to block ER action. Although considered a success, a substantial proportion of these patients will relapse after treatment, often resulting in metastatic disease that cannot be cured. Importantly, in ~80% of all metastatic endocrine-resistant cases, ER continues to be expressed and is still considered the driver. OI Wilbert Zwart (NKI) used Oncode's drug repurposing library to identify vulnerabilities in endocrine-resistant breast cancer cells, potentially revealing new therapeutic options for these patients. Using a carefully set up screening assay, the entire drug repurposing library was tested, resulting in a broad set of compounds with potential tumour cell proliferation inhibiting properties. In a secondary, more focused screen, these compounds were validated, revealing a large subset of compounds that proved to be effective in endocrine-resistant breast cancer cell lines. Closer investigation of the top hits revealed that several of these compounds belonged to a class of drugs known to have an effect on one particular pathway.

Importantly, several of the drugs of interest are already clinically applied in the treatment of other cancers. While it remains untested whether these compounds would be clinically effective in endocrine-resistant breast cancers, the current clinical application of these drugs clearly has the potential to accelerate the route towards clinical trials of the study findings. Zwart is now validating the drugs in cell cultures derived from metastatic breast cancer patients, as well as in patient-derived xenograft mouse models. In parallel, these results have been discussed with the NKI Clinical Trials Unit, who are now designing a clinical trial to confirm the findings in a clinical setting as soon as pre-clinical validations have been successfully completed.

Ruud Delwel's quest to combat AML: The research group of Ruud Delwel (Erasmus MC) is mainly focused on molecular defects driving the development of acute myeloid leukemia (AML). AML is a rare but highly fatal form of leukemia that mostly affects elderly people.

"When you look at AML cells under a microscope, they all look alike. But patients with AML can respond very differently to treatment: There are individuals that respond well to treatment. There's a group that doesn't respond to the treatment at all. Unfortunately, the biggest group of patients respond well to treatment at first, but the cancer comes back after a few years and the outlook for those patients is then very poor", explains Delwel.

At the biological and molecular level, AML is not one disease. Different subtypes with distinct abnormalities can be distinguished based on different genetic defects. For many years, Delwel's group focused on one of the most aggressive forms of AML – one that is driven by overexpression of the EVI1 oncogene. To combat this aggressive form of AML, the Delwel group developed screening assays to identify drugs that can interfere with oncogene overexpression. This is where the Oncode Drug Repurposing programme came into play. Delwel's group was granted a drug repurposing screen, which was performed in 2021 with the help of the Oncode centre of expertise at NKI.

Following an initial drug screen with the library, 100 compounds were selected for a secondary dose response series. Based on the data from these screens several compounds were selected that had an effect on EVI1.

“We will now focus our efforts on understanding the mechanisms behind the action of these compounds. We are very excited to have found several molecules that have an effect on a previously undruggable oncogene, something that may hold great promise for the future treatment of this subgroup of AML patients. Moreover, if one of the compounds proves to be clinically relevant in the future, impact can be made relatively quickly and cost effectively since many of the compounds in the library have been either approved or are in late-stage clinical development for other indications,” says Delwel.

Socially Responsible Licensing of Oncode innovations: Oncode contributed to setting up the Socially Responsible Licensing (SRL) policies and toolkit of the Netherlands Federation of University Medical Centres (NFU) and was one of the first to endorse them. The Socially Responsible Licensing (SRL) guidelines and toolkit offer Dutch knowledge institutions a common basis for discussions with other parties about the future use of their patented knowledge. Along with the usual agreements about rights and obligations, the SRL pays explicit attention to societal objectives, such as the effective availability of products and services.

Since 2019, Oncode has explicitly incorporated SRL principles in its license agreements and has negotiated adherence to the guidelines for agreements in which they are applicable. The table below shows the number of licenses Oncode has brokered during its years of operations, and the number of times the SRL guidelines were fully applicable and subsequently incorporated. It is of note that SRL guidelines are only fully applicable to those agreements relating to therapies or diagnostics (not all guidelines are applicable/relevant to agreements dealing with research or software tools). In 2021, the Dutch Ministry of Health requested an assessment of Oncode’s SRL performance and Drug repurposing activities from Oncode’s IRC. The assessment was completed in February 2022, with the IRC rating Oncode’s performance as ‘Good’ to ‘Very Good’. The IRC noted that: *“although the implementation of SRL language in licenses is at an early stage, Oncode helps to set the agenda on making price an important parameter in the development of therapeutics”*.

Health Technology Assessments: Oncode aims to address the cost effectiveness of drugs at a very early stage in their development. To achieve this, the Oncode TechDev fund has supported early Health Technology Assessments (HTAs) for certain projects. HTAs measure the added value of a new treatment compared to the existing standard of care. It evaluates whether a new drug works better, equally well, or worse than existing alternatives, based on its therapeutic effect, potential side effects, influence on quality of life, and means of administration. In addition, it also assesses the cost implication of a new treatment for the patient and its impact on the healthcare system. HTAs are typically used by health authorities and policy makers as an evidence-based auxiliary method to make reimbursement decisions about new treatments and is therefore usually only implemented by drug developers in the late stages of development. Oncode, in collaboration with Thinc at UMCU, is pioneering the use of HTA analyses at a very early stage of drug development in order to determine a drug’s cost-sensitivity throughout the entire drug development cycle and guide/adjust development routes accordingly. Oncode financed 5 HTA analyses up to the end of 2021, the outcomes of which have helped guide Oncode’s decision process for future project development/investments.

3.3.6 Interview Madelon Maurice

“Without Oncode, Laigo Bio wouldn’t exist”

Molecular cell biologist and Principal Investigator Madelon Maurice not only leads her own research group at the UMC but following a breakthrough discovery in her lab she decided to create her own company as well. What issues are encountered when setting up your own start up as a scientist? And what are ways to navigate these? Madelon Maurice shares her views with Oncode.

You founded Laigo Bio following a breakthrough lab discovery. What did this discovery entail?

“Tumours are caused by problematic cell growth or cell division. This is also the case for the type of cancer my team and I study: colorectal cancer. Changes in communication pathways between cells play an important role in this. Cells ‘talk’ to each other by sending protein ‘messages’ that are in turn received by other proteins – also known as receptors that are located at the cell surface. Upon binding these messages, these receptors will become activated and then start to transmit signals to the interior of the cell, for instance to promote cell growth or to import nutrients. In the case of normal cells, these processes are tightly regulated. Cancer cells misuse these communication routes, however, by inappropriate activation of receptors to drive their own growth. A key strategy of current cancer medicine is therefore to treat patients with drugs that block the activity of such problematic receptors at the surface of cancer cells. Despite major successes, not all cancer patients respond to these treatments or develop resistance to these.”

“Our discovery has led to a different approach: we found a way to induce removal of such faulty receptors from the surface of cancer cells. This was made possible by an earlier discovery we did; the detection of a group of enzymatic proteins that can remove a specific set of receptors from the cell surface altogether and induce their disposal.”

So how did the plan to turn your lab discovery into a medicine come about?

“As we learned more about the underlying mechanisms, I started to wonder whether we could perhaps use such enzymes to remove other, faulty proteins from the surface of cancer cells, to stem tumor growth. To our excitement, this strategy worked. Moreover, as these enzymes belong to a larger family of proteins, each member of this family can potentially be used in our approach, which greatly expands possibilities to target tumour cells.”

“Soon after Oncode’s foundation in 2018, I shared my idea with my Oncode business developers Emil Pot and Amber Liu. They showed great enthusiasm for my idea and our discussions encouraged me to generate the first set of results. We filed for patents and started thinking about the best way to generate

proof-of-concept; to show in a systematic manner that we could direct the activity of this family of enzymes to degrading other harmful proteins.”

“Also, we started to talk to investors. Through Oncode’s network I got in touch with ArgoBio Studio, a company that invests in promising lab inventions. We partnered and jointly founded biotech Laigo Bio in February this year. All in all, Oncode’s guidance and support has been invaluable along the way, without their help Laigo Bio wouldn’t exist, really. Besides, Oncode’s funding support has been equally crucial to get to this stage.”

Can you explain this a bit more?

“When you have an innovative idea, it can be hard to obtain the necessary funding to pursue it without having experimental evidence. Oncode’s base funding is specifically aimed at such ‘high risk, high gain’ research that is intended for pioneering new directions that are risky but, at the same time, may have a huge impact. With Oncode base funding, I could expand my team and generate the first evidence that supported our idea. Thanks to additional support of Oncode’s Technology Development Fund we further validated the idea, by investing in relevant model systems and materials in the lab. By 2019, we could demonstrate that our idea worked. Currently, we are talking to potential venture capital partners and hope to start a first round of clinical studies in the next few years.”

“Besides these entrepreneurial activities, I benefit from being part of the Oncode network in many other ways. What drives me in my work is to find and pursue novel ideas and work together with other groups to make discoveries. Oncode provides plenty of opportunity to do so, by offering you the chance to meet with equally driven scientists from adjacent fields. For instance, thanks to an encounter at an Oncode meeting, my team and I started to collaborate with molecular biologist and Oncode Investigator Michiel Vermeulen and his team to research the mode of action of a novel anti-cancer drug.”

It can be challenging to be a first timer in the business world. What are some of the issues you currently face?

“It can at times be challenging to navigate between different types of interests of all parties involved. Because everything is so new and lots of activities are started at the same time, it can be hard to gauge the future impact of certain decisions, in terms of what it could mean for yourself and your team. It has been very helpful to talk to people who are already more experienced in such dealings. This is another reason why Oncode’s Business Development Unit can make such a difference to starting scientific entrepreneurs.”

“Another challenge lies in the near future. Right now, I am still very much involved in all aspects of the company, as we need to further develop the science part first. Over time, my part will likely be less prominent, and I will have to delegate more and more. Having been so intensively involved in the process from the start, it may prove difficult to let go of the reins.”

What advice would you give to fellow scientists who aspire to setting up their own start up following a ground-breaking lab discovery, but worry this might be too difficult?

“Creating your own start up can be time consuming and challenging. But these challenges pale next to the prospect that your discovery could one day help cancer patients in a significant way. Moreover, I greatly enjoy the energy and excitement coming from doing something really new. So, if your gut feeling tells you that your discovery could make an important contribution to cancer medicine, and this is something you really would like to contribute to, it is worthwhile to explore the idea.”

“Also, entering the world of business does not need to conflict with the pursuit of your overall scientific goals. For instance, our early-stage discussions with investors challenge us on the science behind our discovery, which adds to the quality of our work and our contribution to the field. More generally, my interactions with third parties like investors or other companies have been quite inspirational, leading to new perspectives and ideas. As such, the activities around my company didn’t so much intervene with, but actually strengthened my scientific profile.”

4. Governance and Management

Oncode operates as a ‘virtual institute’, with a small team providing programme management, valorization, general management, and support services to all Oncode researchers in the different partner institutions. Oncode’s staff are guided and supported by its Board and Committees (see Figure below). Oncode’s main governance bodies were installed and initiated their activities in 2017 and 2018.

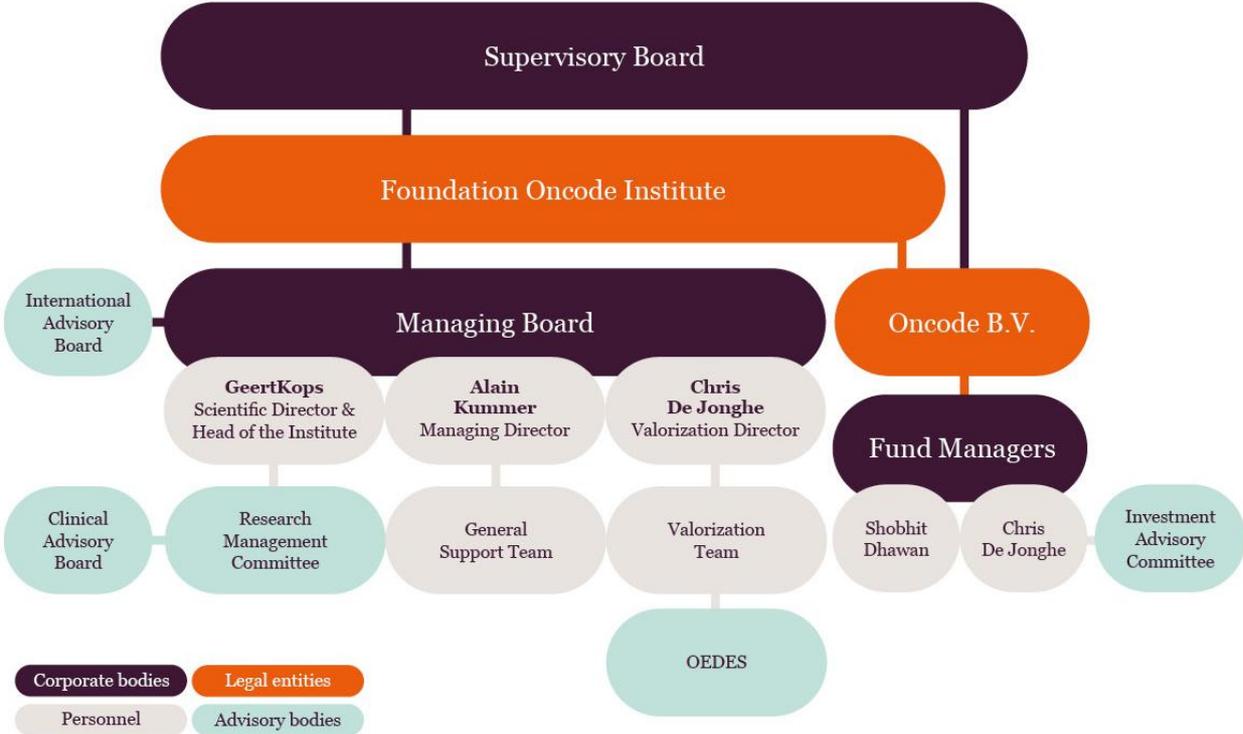


Figure: Oncode Governance structure

4.1 Supervisory Board

The Supervisory Board (SB) supervises and oversees the implementation of Oncode’s overall strategy as well as the general course of its affairs. Members of the SB are appointed by the SB, which must comprise an independent chair (unattached to any stakeholder), one nominee from each of the following Oncode stakeholders – the Dutch Cancer Society (KWF), the participating Dutch Ministries, the Affiliated Research Institutes, and Affiliated University Medical Centres (UMCs) – and two Expert Members. Members of the SB are appointed for a period of four years and may be reappointed only once for a period of four years. The board’s composition in relation to the expertise and background required is determined by the SB in the Oncode SB Profile, which is part of the Oncode Good Governance Charter. Recruitment of the SB Chair and SB Expert Members is conducted through a transparent public procedure.

4.1.1 Current composition of the Supervisory Board

The SB is chaired by Prof. Dr. Eduard Klasen. Currently, its other members are Dr. René Kuijten, Dr. Edvard Beem, Prof. Dr. Ben Feringa, Erica van Wuijtswinkel (Patient Representative), Drs. Johan van de Gronden, Mrs. Tanja Nagel, and Prof. Dr. Stefan Sleijfer.

4.1.2 Supervisory Board Remuneration

Members of the SB do not receive remuneration for their activities, either directly or indirectly. They may, however, be reimbursed for costs related to other services they provide to Oncode. Expenses incurred by the SB Chairman and SB Patient Representative are reimbursed. In 2021, total reimbursement of SB-related expenses amounted to zero.

4.1.3 Report of the Supervisory Board 2021

The SB held six meetings in 2021, during which it discussed and advised on the execution of the Institute's overall strategy with the Oncode Managing Board (MB). Prof. Dr. Hans van Leeuwen, the SB member representing the Affiliated University Medical Centres (UMCs) since January 30, 2020, was replaced on September 1, 2021, by Prof. Dr. Stefan Sleijfer.

During a meeting on November 25, 2021, the SB approved a formal amendment to the articles of association of Oncode that aligns Oncode with the Legal Entities Management and Supervision Act (WBTR), and updated the articles of association with regard to the rotation schedule of the SB. The SB also approved Oncode's updated Good Governance Charter. During 2021, the SB was continuously updated on Oncode's day-to-day progress and implementation of its various programmes and initiatives. The SB was consulted on numerous matters, including the organizational structure and finance of Oncode, the plans and strategy for phase 2, Oncode's mission and vision, the OI assessment process, the Oncode-PACT Growth Fund application, Oncode's targeted programmes supporting science, collaboration and valorization, and matters related to funding.

4.2 Board and committees

Managing Board: The members of the Managing Board (MB) operate and manage Oncode. The managing board's current members are Geert Kops, Scientific Director and Head of Oncode Institute, Chris De Jonghe, Valorization Director, and Alain Kummer, Managing Director.

Research Management Committee: The Research Management Committee (RMC) advises the MB on the content and execution of Oncode's scientific strategy. The RMC is chaired by Scientific Director Geert Kops (Hubrecht Institute), its other members being Madelon Maurice (UMC Utrecht), Jan Paul Medema (Amsterdam UMC), Karin de Visser (NKI-AvL), Thijn Brummelkamp (NKI-AvL), Ruud Delwel (Erasmus MC), Mario van der Stelt (UL), and Chair of the Clinical Advisory Board Henk Verheul (Radboud UMC). The RMC held 10 regular meetings and several focused sessions in 2021. Important topics on the RMC agenda were preparation for the scientific strategy for phase 2, set-up of the OI assessment and selection procedures and the execution of the process itself, and review of the annual reports of the OIs.

Clinical Advisory Board: The Clinical Advisory Board (CAB) provides advice on Oncode's strategy, the operation of Oncode programmes designed to promote translational research and clinical connections, and all applications for funding from the Clinical Proof-of-Concept fund. The CAB is chaired by Henk Verheul (Radboud UMC), its other members being Lianne Bogers (patient representative), Natasha van Eijkelenburg (PMC), Ferry Eskens (Erasmus MC), Mette Hazenberg (Amsterdam UMC), Joop Kroes (patient representative), Ritse Mann (Radboud UMC), Jeanine Roodhart (UMC Utrecht), Muriëlle Sark (patient representative), and Ewout Steyerberg (Leiden UMC). Marleen Kok (NKI-AVL), resigned from her tasks and responsibilities within the CAB. Two new CAB members will start in 2022: Andre Bergman (NKI-AVL) and Sjoukje Oosting (UMCG). In 2021, the CAB reviewed and provided input and advice for 7 CPoC pre-proposals and 3 full proposals. Furthermore, it provided input for the clinical workshops. At the end of 2021, the terms of reference and good governance charter for the CAB were updated and finalized. Oncode was sad to announce that patient representative Joop Kroes sadly passed away in 2021 due to the effects of his disease

International Advisory Board: The International Advisory Board (IAB) consists of Chair Teri Willey (Cold Spring Harbor Laboratory), Richard Marais (Paterson Institute/CRUK), Vishva Dixit (Genentech), Claire Isacke (IRC London), Alberto Bardelli (University of Torino), Sabine Tejpar (UZ Leuven), and Paul Workman (ICR, London). In 2021, Laura van't Veer (UCSF) and Stan Kaye (Institute of Cancer Research) resigned from the IAB and were replaced by Alberto Bardelli and Sabine Tejpar. The board was additionally extended with Paul Workman. Oncode was saddened by the news of the unexpected death of David M. Livingston MD, in October 2021. David had been involved in Oncode since before its launch and over the subsequent years served as chair of the IAB.

The IAB met twice in 2021, firstly to review and discuss the annual report in May, and later in the year to play a pivotal role in the assessment of OIs.

Oncode B.V.: Oncode B.V., which manages the Oncode Oncology Bridge Fund, became operational in April 2019. The Oncode SB functions as the SB of Oncode B.V. The company's Management Board currently comprises Fund Managers S. Dhawan and C. De Jonghe.

5. Management Report

Oncode was founded on 3 pillars: Scientific Excellence, Collaboration, and Valorization together creating impact. 2021 marked the fourth year of Oncode's operations, and during the year the institute was able to capitalize on the activities initiated in previous years while simultaneously preparing itself for the next phase of Oncode. Like 2020, the past year was also marked by the ongoing COVID-19 pandemic. The Oncode community's research activities were largely carried out under 'normal' circumstances, but the social distancing regulations still impacted the ability to meet and interact with people face to face.

5.1 Oncode Operations

Organizational changes:

Managing Board: No major changes occurred in the Managing Board (MB) in 2021. Currently the MB consists of Chris De Jonghe (Valorization Director), Geert Kops (Scientific Director and Head of Oncode Institute), and Alain Kummer (Managing Director).

Management team: No major changes occurred the Management Team (MT) which currently comprises Oncode's 3 directors plus Ester Frische (Head of Research and Community), and Tale Sliedrecht (Head of Strategy).

New recruits and operations during COVID-19: In 2021 Alina Boca- Eichner was recruited as Data Entry Assistant to assist the valorization team, and Soumela Kasperiouk was recruited as Management Assistant. The Oncode office remained operational throughout the 2021 lockdown periods, with all valorization and programme management activities continuing while staff worked from home or, when social distancing regulations allowed, at the office in Utrecht.

International Advisory Board: In 2021, there were multiple changes to Oncode's International Advisory Board (IAB) membership. Laura van't Veer (UCSF) and Stan Kaye (Institute of Cancer Research) resigned from the IAB and were replaced by Alberto Bardelli (University of Torino) and Sabine Tejpar (UZ Leuven), and the board was extended with the appointment of Paul Workman (ICR, London). Oncode was saddened by the news of the unexpected death of David M. Livingston MD in October 2021. David had been involved in Oncode since before its launch and during its years of operations served as chair of the IAB. He was succeeded as chair by Teri Willey.

Entrepreneurs in Residence: Like 2020, Dr. Allard Kaptein, Dr. Markwin Velders, and Dr. Dirk Pollet acted as 'Entrepreneurs in Residence' (EIR). No additional appointments were made to the EIR in 2021.

Changes within the Oncode research team: In 2021, Edwin Cuppen (UMC Utrecht) announced that he was taking on the role of full-time Scientific Director of the Hartwig Medical Foundation, consequently stepping down as professor at UMC Utrecht and ceasing all his research activities. As a result, Cuppen will no longer be an OI. Within UMC Utrecht, Cuppen's close colleague Jeroen de Ridder will now oversee the Cuppen

research group and their research activities. The Oncode valorization team will ensure that legal obligations and projects initiated prior to Cuppen's departure will continue to receive Oncode support.

Impact of the COVID-19 pandemic: Throughout 2021, Oncode, like the rest of the world, was impacted by the COVID-19 pandemic. Research activities within the Oncode labs, compliant with the social distancing guidelines set by the Dutch government, were maintained. In 2020, Oncode performed a risk analysis that showed the impact of the pandemic, although substantial, was manageable. Due to adjustments made in 2020, the impact of the COVID-19 pandemic in 2021 was minimal, with research activities (including clinical trials) progressing as expected.

For Oncode activities, no major impact on the day-to-day activities of the valorization funds and targeted programmes was observed. Oncode meetings sometimes had to adapt to social distancing guidelines, opting for a hybrid or fully digital format rather than normal face-to-face interaction. In addition, Oncode business developers were sometimes limited in their ability to attend (inter)national meetings and were less frequently able to visit the Oncode labs due to social distancing regulations.

Oncode observed a decrease in research funding obtained by OIs during the first year of the pandemic. This downward trend continued in 2021. Some funding calls by major (inter)national funding agencies were cancelled, postponed, or decreased in size, but we are not yet in a position to conclude that the decrease in funding obtained by OIs is solely caused by the pandemic, and therefore only temporary, or whether it is a structural problem. Oncode will continue to monitor the funding situation in the coming years.

5.2 Oncode finances

Although the COVID-19 pandemic has continued longer than expected, its impact on the Oncode laboratories and Oncode's activities in general was limited, as predicted by our 2021 risk analysis. There are few OIs that reported a (limited) delay to spending their base funds due to the pandemic. For the Oncode's operational activities, the results during 2021 only show a minor COVID-19 related reduction in spend, mainly on travel and the organization of meetings and conferences.

As a result of pre-2021 delays due to the shut-down of some laboratory operations due to COVID-19, budget-neutral extensions are being arranged with the relevant funding organizations so that certain funds can be used beyond the original end date of phase 1 (31 August 2022) until at least the end of 2022.

The MB has obtained a verbal commitment from all funders to fund phase 2 of Oncode Institute and the relevant funding agreements are now being prepared for signature by all parties before the end date of phase 1. New affiliation agreements with the partner institutions are also being prepared with all investigators who will be invited to participate in phase 2 having been informed.

On this basis there is a high level of confidence that Oncode can make a successful transition from phase 1 to phase 2, and the annual accounts have been prepared on this assumption.

In 2021 Oncode, together with other parties, submitted a proposal called Oncode-PACT to the Netherlands National Growth Fund. The proposal met all the requirements and in April of 2022 it was announced that the proposal would be granted National Growth Fund funding. Oncode Institute has positioned itself as the institute that will execute operational implementation of this initiative and will be responsible for financial execution of the subsidy. The subsidy is for € 325 million over 8 years, with € 161 million being awarded directly and a further € 164 million euros being awarded conditionally.

Base funding: OIs were alerted to the fact that a limited downward adjustment of their base funds may be necessary in 2022. The amount will be determined in Q1 2022, when we have better insight into potential financial windfalls.

5.3 Programmes, Funds, Events

In 2021, Oncode continued to build on the strong foundations that were laid in the first years of operations. The focus of Oncode's management team in 2021 was on maximizing the output of the operations and activities set in place.

Within the Infrastructure & Technologies (I & T) programme, no new major investments were made. However, as part of the set-up of several facilities (the Drug Repurposing and Oncode Therapeutic Antibody facilities) individual research projects were awarded. Oncode undertook various activities to ensure maximum usage of its new facilities and infrastructures by, among other actions, promoting them via its communication channels and organizing masterclasses.

The CPoC programme awarded funding for 4 new projects to OIs and their collaborating clinicians. In addition, 1 CPoC project was completed in 2021. The CPoC programme was one of the programmes quite severely impacted by the COVID-19 pandemic in 2020. However, all projects that were delayed or postponed were reinitiated in 2021 and no further major impact was reported throughout the year. For the projects that were delayed in 2020, Oncode has adjusted the expected timeline and milestone achievement dates for each individual project. Lastly, due to social distancing regulations, only one clinical workshop was held in 2021. It is expected that Oncode will be able to host more of these workshops in the coming years.

The Drug Repurposing programme gained more and more attention since its initiation in 2019. The programme awarded 6 screening programmes in 2021, bringing the total number of projects to 14. Furthermore, the first screening programmes from previous years were completed.

The Patient Engagement (PE) programme set up a patient-researcher 'partner' system in 2021 designed as a steppingstone to further integration of the patient perspective into the Oncode community. In 2021, the programme gained more traction with multiple new research groups joining it. While the COVID-19

pandemic did limit face-to-face meetings from time-to-time, the programme and its participants adapted to the situation by using digital meetings to maintain frequent interaction with each other.

The Technology Access (TA) programme was launched in 2021 as a pilot programme. With advice from the RMC, a programme strategy was drafted for the remaining year of phase 1. With an adjusted budget, a call was set up to facilitate the funding of 3 initiatives being executed in 2022. Based on learnings from the pilot programme, the TA programme will be revised and more closely defined for implementation in phase 2.

Open Science and FAIR Data (OSFD) programme: In 2021, the OSFD programme advanced its commitment to knowledge sharing within the Oncode and wider community by organizing workshops, communicating best practices, and establishing connections with the research data management support teams in different Oncode research institutes.

Training and Mentoring programme: Oncode's training programme focuses on organizing science-driven, technical masterclasses and valorization training using a practical learning approach. In 2021, Oncode hosted 5 masterclasses, organized in collaboration with OIs and the Technology & Infrastructure programme. Two planned masterclasses were postponed to 2022 due to COVID-19 restrictions.

In 2021, Oncode offered peer support sessions to junior investigators who participate in The Mentoring programme. These sessions are facilitated, interactive peer consulting sessions in which junior investigators share practices in small groups and learn new approaches to dealing with common challenges they face as a research group leader.

Meetings and Events: To support the Oncode community in sharing their knowledge and expertise and discussing new developments, Oncode organized several meetings throughout 2021 on a diverse set of topics. Even though the pandemic still had a big impact on planned activities, Oncode adapted to the situation and continued its activities either fully online, in a hybrid setting, or where possible, face to face. In total Oncode hosted 10 meetings with a total of 1250 participants.

5.4 Valorization activities, programmes, and funds

Despite the ongoing COVID-19 pandemic and the resulting social distancing regulations, Oncode business developers were able to maintain close contact with research teams in Oncode's partner institutions. Their proactive valorization approach led to many new agreements and public private collaborations (see section 3.2.3). Based on its valorization performance indicators, Oncode is now exceeding the yearly targets set at the launch of the institute.

Through its Industry Engagement (IE) programme, Oncode aims to engage and partner with the best industry players in the field. The IE programme therefore relies heavily on relationship building and one-to-one communication. While increasingly more (inter)national events have been hosted throughout 2021, the ongoing COVID-19 pandemic still drastically reduced the opportunity to meet potential new BioPharma leads and nourish existing relationships. The newly widespread adoption of digital meetings has however

facilitated interactions between industry and investigators at a global scale. Through dedicated on-line partnering meetings, Oncode was able to organize more than 30 meetings between OIs and industry partners during 2021. In total the Oncode valorization team members participated in more than 150 partnering meetings with industry partners.

Oncode's Strategic Funding Support (SFS) programme is aimed at helping OIs navigate the funding landscape and thereby boost Oncode's research funding. The programme provides tailored funding strategies for OIs and spin-off companies. In 2021, Oncode revised this strategy to create a more balanced utilization of resources, choosing to focus its attention on support through grant reviews and by providing (outsourced) support for strategic projects. Using this amended strategy, the programme successfully met its objectives for 2021 – the programme achieved a success rate of 52% (compared to 35% last year), in total securing €17.4M of funding.

The Oncode Intellectual Property (IP) Fund supports the filing and prosecution of intellectual property protection, primarily in the form of patent or trademark filings made by the Valorization Team. In 2021, €322.784 was deemed as IP expenses eligible for reimbursement from the fund. In 2021 the Valorization Team filed 19 priority patent applications, 12 PCT patent applications, 7 national phase applications and 1 trademark. Oncode ended 2021 with an active patent portfolio of 50 patent families.

The Oncode Technology Development Fund (TechDev fund) was established to address scientific, technical, and business issues with the aim of increasing the likelihood that Oncode inventions are licensed and further developed. The fund is managed by the Valorization Team and all projects are directly associated with an Oncode invention. Projects include activities such as drug target validation, high throughput screening, medicinal chemistry, toxicology studies, AD/PK studies, the formulation of drugs to support CPOC clinical trials, and health technology assessments (HTAs). With a total budget of €4M, the fund has so far funded 24 projects, of which 7 were awarded and 6 were completed in 2021.

The Oncode Oncology Bridge Fund, managed by Oncode B.V., is an investment fund of €7.2M that provides pre-seed and seed capital to commercially viable enterprises originating from within the Oncode community to help them translate their research ideas into market-ready investment opportunities. Early-stage investments are accompanied by professional intellectual property management, pre-investment technology de-risking, and, where possible, preliminary clinical validation. Additionally, the Bridge Fund prepares new enterprises for follow-on investments from private investors such as business 'angels' or venture capitalists. Oncode B.V. has committed €1.1M of investment capital in 7 spin-off companies, which currently employ a total of 17 FTEs. In addition, 8 projects are in either an ideation or validation phase. In 2021, the Oncode Bridge Fund committed €600K of investment capital in 2 spin-off companies, and provided follow-on financing to Imogene B.V..

Oncode is mindful of the need for new innovations in cancer therapy to reach patients at an affordable price and has therefore set up its Affordable Health Care (AHC) programme. While Oncode cannot solve affordability problems on its own, it aims to contribute to the affordability of new medical solutions originating from Oncode.

Oncode's activities regarding AHC are accommodated in several other Oncode activities, including support for 3 CPoC studies specifically focused on AHC. Via its [DR programme](#), Oncode stimulates drug repurposing research that has the potential to identify novel indications for known drugs and compounds. In 2021, the DR programme approved 6 screening projects. Lastly, Oncode has committed to conduct all its licensing activities within the framework of the Socially Responsible Licensing (SRL) guidelines and toolbox produced by the NFU. Oncode is one of the first organizations to test the guidelines and use the tool kit in practice. In 2021, Oncode processed 9 licences, 5 of which were subject to the SRL guidelines. SRL licenses were not applicable to the other 4, since these either deal with in-licences, IP rights to Oncode affiliates for R&D use, or option agreements.

5.5 Review of strategic plan phase 2 & OI assessment

As described in Oncode's general monitoring and assessment procedures, Oncode's IRC will review the phase 2 strategic plan and the assessment of OIs in 2022. During 2021, Oncode started preparing for the IRC's upcoming site visit. The phase 2 strategic plan was drafted and discussed with the relevant funders, and the OI assessment procedure was set up and approved by the SB. The procedure was executed in the second half of the year and will be finalized in 2022. To ensure an efficient and effective IRC site visit in 2022, Oncode's MB planned multiple pre-meetings with the IRC in 2021 to discuss the assessment and other tasks in hand.

5.6 Research Management Committee

In early 2021, Oncode's Management Board (MB) asked the Research Management Committee (RMC) to set up a fair, transparent OI assessment procedure. During 2021, an assessment was performed for all senior OIs and junior OIs who started in 2017 (45 OIs in total) via a stringent, transparent review process that involved external reviewers and the RMC. OIs were evaluated on **a)** their scientific excellence, and **b)** their contribution to Oncode's goals (e.g. valorization, collaboration, and community activities). A final decision on the assessment outcomes will be made in 2022 by the MB after reviewing advice from Oncode's IAB and IRC. The 12 junior OIs who started in 2019 will continue as juniors and will be evaluated after having been with Oncode for 4 years, which means in early 2023.

In 2020, the RMC reached out to the Oncode research community to contribute to the scientific strategy for phase 2. Specifically, the RMC wanted to make optimal use of Oncode's unique set-up to accelerate discoveries by forging highly innovative, large-scale collaborative projects centred around specific scientific or clinical challenges. A call for proposals for these *Oncode Accelerator Projects (OAPs)* resulted in the submission of 23 initial proposals from (teams of) OIs. These were discussed in an online OI retreat, with proposals identified as synergistic combined and resubmitted for review. After review by the IAB and RMC, 3 projects were selected for inclusion in Oncode's phase 2 strategy. Of these 3 OAPs, two projects have already been successful in attracting funding through external (private) funding sources.

6. Key Performance Areas

Key Performance Area 1 (KPA1) : Scientific Excellence

The scientific excellence of Oncode is seen as a measure of the organization's effectiveness in creating an environment in which Oncode researchers can reach their maximum innovation potential, through effective implementation of the scientific strategy. The added value of Oncode's unique set of activities and the access it provides to unrestricted funding compared to conventional research funding will be evaluated by illustrative examples. These examples and supporting quantitative data will be used specifically to assess Oncode's ability to:

- promote innovative basic and pre-clinical research lines of high quality, beyond that which could reasonably be achieved by regular funding mechanisms, in alignment with Oncode's research themes.
- accelerate discoveries by creating access to novel technologies, and high-end infrastructures, facilities, and equipment.
- attract and develop the future leaders of oncology research.

KPA1 2021 Update: Throughout 2021, Oncode continued to support its community to ensure high quality basic and preclinical research. Oncode's base funds are highly valued by OIs as they provide them with the ability to initiate research lines that would otherwise be difficult to finance due to a lack of preliminary data or track record. Of equal importance, the funds provide OIs with the flexibility to accelerate research lines and change the scope of research programmes. The impact of Oncode's base funds can be seen at a multitude of levels, such as publications and new funding opportunities. Ample examples of what has been achieved can be viewed in section 3.1.1.

While Oncode did not make major investments in new research facilities in 2021, it did promote its facilities through its communication channels and technical workshops to showcase the available expertise and technical capabilities of the various facilities. Lastly, a pilot Technology Access programme was initiated with the aim to provide the Oncode community with access to emerging technologies that have the potential to be of high value for the wider Oncology network.

Key Performance Area 2 (KPA2): Collaborative Excellence

The collaborative excellence of Oncode is seen as a measure of the quality of execution of the organization's strategy to drive innovation through collaboration, based on the potential of the Oncode community and the strategy to build a scientific community in which interdisciplinary collaborations are natural, boundaries to collaborate are overcome, and a culture of openness and sharing is fostered. Collaborative Excellence will be evaluated by presenting illustrative examples. The examples and supporting quantitative data will be used specifically to assess Oncode's ability to:

- create innovative research initiatives by facilitating and promoting collaborations within the Oncode community.
- create a research ecosystem in which collaborations between clinical and basic research groups are stimulated and rewarded.

- drive the development of research findings into potential applications through innovative public-private partnerships.

KPA2 2021 Update: As in previous years, Oncode organized a wide range of meetings to facilitate novel interactions between scientists from different backgrounds and with different expertise. While the ongoing COVID-19 pandemic caused Oncode to postpone some meetings, Oncode was successful in providing the community with a wide variety of events and meetings, either face-to-face, hybrid or fully online. Examples include Oncode’s institute-wide meeting, small-scale technical masterclasses, and meetings with industry partners (section 3.2.1). Furthermore, many Oncode funding programmes require joint applications by multiple OIs (for example, the newly initiated TA programme, section 3.1.3) or collaboration with a clinician (CPoC programme, section 3.3.2). Lastly, our Industry Engagement efforts and Strategic Funding Support programme (section 3.3.4) led to many new (international) public-private partnerships (section 3.2.3).

Key Performance Area 3 (KPA3): Patient benefit

Patient benefit is seen as a measure of the quality of the execution of the strategy to fulfil Oncode’s ultimate aspiration to translate Oncode research findings into benefits for patients. Oncode’s clinical capabilities will be evaluated by presenting illustrative examples. The examples and supporting quantitative data will be used specifically to assess Oncode’s ability to:

- implement an effective CPoC program that ultimately generates innovative clinical studies based on findings by OIs.
- set up and efficiently utilize a high-quality valorization infrastructure to increase the societal impact, including unmet medical needs, of Oncode research findings.
- provide OIs with the tools, funds, and network to effectively translate basic scientific findings into potential applications that solve unmet clinical needs.

KPA3 2021 update: Oncode was pleased to see that a flow of high-quality projects continued to find its way towards the CPoC programme in 2021. Four new projects were awarded in 2021, bringing the total to 17 (section 3.3.2). To increase its ties with clinicians, Oncode aims to organize multiple clinical workshops in 2022, making up ground for the single clinical workshop that was held in 2021. Another had to be postponed due to the ongoing impact of the COVID-19 pandemic.

The translation of Oncode research findings into benefits for patients is also supported through the Oncode valorization infrastructure. By engaging with industry, and through the TechDev (section 3.3.1) and Oncology Bridge funds (section 3.3.3), Oncode supports the translation of research innovations into tangible products for patient benefit. In 2021, this resulted in 2 new spin-off companies being created.

Lastly, in a pilot of Oncode’s Patient Engagement programme, 11 (ex)patients were connected to Oncode research groups (section 3.2.2).

Key Performance Area 4 (KPA4): Economic benefit

The economic benefit of Oncode is seen as a measure of the ability to translate the Oncode community’s research findings into economic benefits in terms of revenues, investments, and jobs. Oncode set itself an

ambitious 15-year goal in which every publicly invested euro will be matched with one euro of private investment either directly in Oncode or in Oncode spin-off companies. The economic benefit created by Oncode will be evaluated by presenting illustrative examples of the value created by Oncode's establishment of an ecosystem and activities that drive economic benefits. The examples and supporting quantitative data will be used specifically to assess Oncode's ability to:

- set up and efficiently utilize a high-quality valorization infrastructure to increase the economic impact of Oncode research findings.
- leverage the investments made by KWF and the Dutch government with 0.5 euro of private investment per euro in the first 5 years.

KPA 4 2021 update: In 2021, Oncode's valorization team supported the translation of research findings into economic benefits through the Oncode TechDev fund, which funded 7 new projects (section 3.3.1). Two new spin-offs were created via the Oncology Bridge Fund (section 3.3.3) and 25 grant applications were submitted, with a success rate of 52% (section 3.3.4), via the Strategic Funding Support programme. Furthermore, Oncode applied SRL guidelines to 5 new licenses and provided its drug repurposing library to researchers both inside and outside Oncode.

Oncode currently leverages the investments made by KWF and the Dutch government with €0.42 euro in private investments per euro after 4 years of operations.

Key Performance Area 5 (KPA5): Affordable Health Care (AHC)

Oncode is mindful of the need for new innovations in cancer therapy to reach patients at an affordable price. To contribute to the affordability of new medical solutions, a significant part of its strategy is focused on achieving this goal. As part of its strategy, Oncode aspires to ensure that within 15 years, 20% of the Oncode community's research findings that reach clinical practice will have emanated from the Oncode AHC programme.

The AHC programme will be evaluated by presenting examples illustrative of Oncode's success in creating an ecosystem in which research ideas can be translated with maximum societal benefit at affordable cost. The examples and supporting quantitative data will be used to assess Oncode's ability to:

- ensure that all licensing activities are conducted within the framework of the Socially Responsible Licensing (SRL) policy of the NFU, which Oncode endorses.
- ensure that at least 20% of Oncode's clinical trial projects in the first 5 years are focused on either personalized medicine (patient stratification) or drug repurposing.
- contribute to the affordability of healthcare by allocating a significant portion of Oncode funding and activities to the promotion of drug repurposing and precision medicine research.

KPA 5 2021 Update: Oncode safeguards the affordability of its innovations by conducting all its licensing activities within the framework of the SRL policy of the NFU, which Oncode endorses (section 3.3.5). Within its clinical activities, Oncode has so far funded 3 CPoC projects (23% of total portfolio) that specifically focus on promoting AHC (section 3.3.5). On assessment of its total CPoC portfolio, it was concluded that of the 17 awarded CPoC projects, 10 projects focused either on drug repurposing or patient stratification, thereby

falling within the scope of AHC. Oncode has set up a Drug Repurposing Programme (section 3.3.5) to stimulate research targeted at repurposing abandoned, off-patent, or patent expiring drugs. The programme up to and including 2021 has awarded a total of 14 screens, including 3 from outside Oncode. Lastly, Oncode aims to address the cost effectiveness of drugs in development at a very early stage in their development. To this end, the Oncode TechDev fund has supported early Health Technology Assessments (HTAs) for certain projects. HTA is an effective means to measure the added value of a new treatment compared to the existing standard of care. Oncode has financed 5 HTA analyses, the outcomes of which have helped guide Oncode's decision process for future project development/investments.

Key Performance Area 6 (KPA6): Organizational & Managerial Efficiency

Organizational & Managerial Efficiency is seen as a measure of **a)** the ability of the organizational set up and governance of Oncode to execute the strategy outlined in the strategic plan, and **b)** the efficacy of the management strategy to monitor and manage Oncode's activities and goals and adjust its strategy when required. Organizational & Managerial efficiency will be evaluated on Oncode's ability to:

- create and demonstrate synergy and coherence between Oncode's programmes and themes.
- set up relevant monitoring processes to enable Oncode's management to adjust activities if needed in order to achieve the Institute's strategic objectives.
- set up an efficient assessment strategy to provide the IRC with sufficient insight into the institute's set up and strategic activities to enable the IRC to fulfil its assessment role.

KPA 6 2021 Update: In 2021, Oncode set up and executed a formal assessment for the larger part of its OI team to determine the make-up of the OI team progressing into phase 2. This assessment will officially be concluded in 2022 following advice from Oncode's IAB and IRC. Furthermore, Oncode's MT has prepared its phase 2 strategic plan in alignment with Oncode's funders and, more importantly, engaged with its funders to ensure financial continuity into phase 2. Oncode will finalize these activities in 2022 by setting up phase 2 funding agreements with its funders and affiliation agreements with its partner institutes.

Appendix I

Boards, teams, and groups

GENERAL SUPPORT TEAM

THE VALORIZATION SUPPORT TEAM

NETWORK OF CONSULTANTS

OPEN SCIENCE AND FAIR EXPERT GROUP

INTERNATIONAL ADVISORY BOARD

INTERNATIONAL REVIEW COMMITTEE

General Support Team

Elize Brolsma, *Project Communications Manager* (Lygature)
Dr. Alexander Duyndam, *Communications Manager* (Lygature)
Tracey Faase, *Financial Controller* (Lygature)
Dr. Ester Frische, *Head of Research and Community support*
Denis Groot, *Financial Controller* (Lygature)
Dr. Colete ten Hove, *Programme Manager*
Vesna de Jong, *Digital Communications Manager* (Lygature)
Soumela Kasperiouk, *Management assistant (since April 2021)*
Emanuela Lonardi, *Programme Coordinator*
Bianca-Olivia Nita, *Project Communications Manager* (Lygature)
Dr. Tale Sliedrecht, *Head of Strategy* (Lygature)
Marlinde Smit, *Programme Manager* (Lygature)
Dr. Jacqueline Staring, *Programme manager* (Lygature)
Dr. Inga Tharun, *Programme manager* (Lygature)

The Valorization Support Team

Dr. Saharla Ahmed, *Business Development*
Ian Bell, *Business Development*
Dr. Shobhit Dhawan, *Fund Manager*
Alina Boca- Eichner, *Data Entry Assistant (since January 2021)*
Dr. Veerle Fleskens, *Business Development*
Amber Liu, *Business Development*
Dr. Yuva Oz, *Business Development*
Emil Pot, *Business Development*
Dr. Alexander Turkin, *Business Development*
Mariëlle Veldhuizen, *Paralegal, Valorization Coordinator*
Dr. Koen Verhoef, *Business Development*

Network of Consultants

Dr. Danny Burg (D2team), *Drug Development Specialist*
Dr. Geert Frederix (UMC Utrecht), *Health Technology Assessment Specialist*
Dr. Ellen Hulskotte (Curare Consulting), *Clinical Trial Design Specialist*
Dr. Paul de Koning MD (de Koning coaching & consulting), *Drug Development Specialist (Retired April 2021)*

Drug Repurposing Advisory Board

Mario van der Stelt (Leiden University)
Roderick Beijersbergen (NKI)
Paul Geurink (LUMC)
Saman Honarnejad (Pivot Park Screening Centre)
Ellen Hulskotte (CURARE consulting)
Wilbert Zwart (NKI)

International Advisory Board

Teri Willey (Chair), VP for Business Development & Technology Transfer - Cold Spring Harbor Laboratory

Prof. Vishva Dixit, Genentech

Prof. Clare Isacke, ICR London

Prof. Richard Marais, Director of the CRUK Manchester Institute

Prof. Alberto Bardelli, Department of Oncology, University of Torino

Prof. Sabine Tejpar, UZ Leuven

Prof. Paul Workman, ICR London

Independent Review Committee

Prof. Susan Gasser PhD (Chair), Director emeritus Friedrich Miescher Institute

Prof. Josep Tabernero MD PhD, Medical Oncologist, Head of Medical Oncology at Vall d'Hebron University Hospital and Director at Vall d'Hebron Institute of Oncology (VHIO)

Prof. Liesbeth de Vries MD PhD, Medical Oncologist, Department of Medical Oncology UMCG

Prof. Richard Marais PhD, Director of the CRUK Manchester Institute & Onco International Advisory Board member

Derek Waddell, Founder & CEO of 81C Limited

Prof. Ivan Dikic, MD PhD, Director Institute of Biochemistry II, Goethe University Frankfurt

Dr. Tim Wells, CSO Medicines for Malaria Ventures & Non-Executive Director at Kymab Ltd.

Appendix II

Oncode in Numbers

ONCODE COMMUNITY

ONCODE OUTPUT

CLINICAL PROOF-OF-CONCEPT PROJECTS

TECHNOLOGY DEVELOPMENT PROJECTS

EQUIPMENT & INFRASTRUCTURE FUNDED PROJECTS

MEETINGS IN 2021

FOLLOW UP FUNDING ORIGINATING FROM BASE FUND RESEARCH

Oncode Community

Position	#	female/male
Oncode research community (31 Dec'20)	923	470/453
Oncode Investigators	43	9/34
Oncode Junior Investigators	18	8/10
Oncode Post docs & Senior Scientists	264	147/117
Oncode PhD students	369	208/161
Oncode technicians & supporting staff	230	128/102
PhD defences	40	20/20

Oncode Output

Publications	#	compared to baseline
Publication all OIs	443	311
Median impact factor all OIs	12.5	8.4
Co-publications with industry	70	36
Open Access (OA) publications all OI	345	203
Share of OA of total publications	78%	65%

Note: Reported bibliometric numbers are based on the sliding window principle (as further detailed in metric report). Briefly: The reported data covers publications from a three-year window, the reporting period year (2021) and the two-years preceding it (2019 and 2020). By using this 'sliding window', Oncode obtains a more robust estimation of the publication activity and citation impact of the publications by OIs.

Agreements	#	compared to 2018
Non-disclosure agreements	108	22
Research agreements	35	7
Material transfer agreements	75	13
License agreements	9	*
Other	20	25
*no baseline data available		

Invention Disclosures	#	compared to 2018
New invention disclosures	35	32
Legacy files	0	11
Non-Oncode	1	*
Portfolio Dec 31	98	43
*no baseline data available		

Patents	#	compared to 2018*
Priority filings	19	9
PCT filings	12	6
National filings	7	7
*no baseline data available		

New Ventures

Single Cell Discoveries B.V. (2018)
Cyclomics B.V. (2019)
Immagene (2020)
Lumento (2020)
Oncosence (taken up as an Oncode portfolio spin-off in 2021)
LiagoBio (2021)

Funding

	€	Compared to baseline
Total Funding attracted (incl. Oncode funding)	€61.2 million	€43.6 million
Total private funding attracted	€10.1 million	€5.12 million

Communication

Community Platform - Statistics 2021:

- 2,914 visitors generated 4,489 sessions and 9,807 pageviews
- 1,089 terms were edited within individual profiles
- 19 clicks for contact (email, LinkedIn, PubMed, phone)

Website statistics 2021:

- 28,652 visitors created 44,206 sessions, resulting in 106,416 page views

LinkedIn

- 4,477 followers on December 31st, 2021
- 889 new followers with a 4.57% engagement rate

Clinical Proof-of-Concept Projects update 2021

Newly-funded CPoC Projects

Mechanism of response and resistance to neoadjuvant PD-1 checkpoint blockade in vulvar squamous cell carcinoma.

Main applicant: Sjoerd van der Burg, LUMC

Funds awarded: € 663K

Year awarded: 2021

New epigenetic combination therapy testing for BAP1-deficient mEsoTheLioma, a double-arm prospective non-comparative phase I/II trial (BEETLE).

Main applicant: Maarten van Lohuizen, NKI

Funds awarded: € 799K

Year awarded: 2021

Tasquinimod as new treatment option in heavily pretreated patients with Myeloproliferative Neoplasms associated with bone marrow fibrosis

Main applicant: Rebekka Schneider, Erasmus MC

Funds awarded: € 511K

Year awarded: 2021

Maximizing treatment options for recurrent glioblastoma patients by whole genome sequencing-based diagnostics

Main applicant: Edwin Cuppen, UMC Utrecht

Funds awarded: € 745K

Year awarded: 2021

Completed CPoC Projects in 2021:

HDAC inhibitor vorinostat in resistant BRAF V600 mutated advanced melanoma

Main applicant: Rene Bernards, NKI

Technology Development Projects

PREDICATE - Towards precision medicine for colorectal cancer patients

Main applicant: Louis Vermeulen (Amsterdam UMC)

Funds awarded: € 150K

Validation of the FUNsice pipeline by target discovery and validation for metastatic colorectal cancer

Main applicant: Miao Ping Chien (EMC) & Louis Vermeulen (Amsterdam UMC)

Funds awarded: € 150K

Validation of the MISC-seq technology in paediatric rhabdoid tumours

Main applicant: Jarno Drost (PMC) & Jop Kind (Hubrecht Institute)

Funds awarded: € 90K

Gut restricted BMP inhibitors to treat metabolic diseases

Main applicant: Hans Clevers (Hubrecht Institute/PMC)

Funds awarded: € 148K

Live-cell screening for disruption of oncogenic condensates

Main applicant: Boudewijn Burgering

Funds awarded: € 150K

Development of DNA ligase III inhibitors to enhance response and overcome resistance to PARP inhibitors

Main applicant: Jos Jonkers (NKI)

Funds awarded: € 150K

Completed Projects in 2021

EZH2 + FGFR inhibitor Combination Therapy to Treat BAP1 Deficient Tumors

Main applicant: Maarten van Lohuizen (NKI)

Validation and optimization of Ultra-wide Field-of-View Optical Microscopy technology

Main applicant: Miao Ping Chien (Erasmus MC)

Turning Mutations into Patient Specific Biomarkers to Guide Personalized Treatment of Ovarian Cancer

Main applicant: Jos Jonkers (NKI)

Preclinical proof-of-concept studies of advanced lipid metabolism inhibitors

Main applicant: Mario vd Stelt (Leiden University)

Establishing AGN192403 as a first-in-class, orally-available PD-1 inhibitor

Main applicant: Daniel Peeper (NKI)

Repurposing BACE1 Alzheimer's inhibitors for immunotherapy

Main applicant: Daniel Peeper (NKI)

Infrastructure & Technologies Funded Projects

No Major investments were made within the I & T programme in 2021

Follow up funding originating from base fund research

Oncode base funds provide OIs with the ability to quickly adapt their approach and allocate funds towards promising new findings. The preliminary data created by these base fund projects have already led to many successful national and international grant applications. All grants that have been obtained on the basis of Oncode base fund research are listed below.

KWF research grant, €818K

Oncode Investigator: Reuven Agami (NKI)

Motivation: All the projects related to aberrant protein production, sloppiness in mRNA translation, and substitutants were mostly financed by Oncode. Because of the availability of Oncode funding, we could push forward investigating this novel phenomenon. Starting from June 2021, we received dedicated support from KWF for Sloppiness and pursued this line of research through this route.

NWO, ENW-Klein grant: €720K (awarded in 2020)

Oncode Investigator: Michiel Vermeulen (Radboud University)

Motivation: The initial interaction proteomics datasets we generated, supported by Oncode base funds, served as a basis for an EMBO long-term post-doc fellowship (awarded to K. Kliza) and an ENW-KLEIN2 project in collaboration with Dima Filippov.

ODAS foundation: €355K

Oncode Investigator: Den Boer (PMC)

Motivation: We used the Oncode base fund to pioneer these types of immunotherapeutics/niche studies, generating (pilot) data to gain expertise and show proof-of-concept for this innovative field of research. In 2021, additional funding was secured (ODAS grant) for this research, which is performed in collaboration with the tumor immunologists and CAR-T/immune-therapists in our center.

ZonMw open competition: €750K

Oncode Investigator: Peter ten Dijke (LUMC)

Motivation: Our expertise/insights and broad array of innovative cellular assays have provided the basis for ZonMW open competition (funded) and other grant applications (pending).

KWF research grant: €714K

Oncode Investigator: Jurian Schuijers (group Boudewijn Burgering (UMC Utrecht))

Motivation: The work performed within the frame of Oncode provided the preliminary data that enabled a successful application for a KWF grant by Dr Jurian Schuijers.

KNAW research grant: €250K

Oncode Investigator: Jop Kind (Hubrecht institute)

Motivation: Our Oncode base fund allowed us to further develop a method to generate proof-of-concept. Based on these pilot experiments, we have now secured funding from a KNAW research fund (250k) to further develop the project in collaboration with Jan Paul Medema.

NWO Vidi grant: €800K

Oncode Investigator: Jarno Drost (PMC)

Motivation: In collaboration with the De Wit group, we found that derailed enhancer landscapes drive oncogene expression in MRT. A manuscript describing our findings is currently in preparation. This base fund project provided preliminary data that was included in my NWO Vidi proposal.

KWF research grant: €420K

Oncode Researcher: Susanne Lens (UMC Utrecht)

Motivation: Research conducted using Oncode base funds has allowed me to gather preliminary data for a new idea and method that supported the successful application for a KWF research grant.

NWO consortium grant: €3.5M

Oncode Investigator: Jop Kind (Hubrecht Institute) and Michiel Vermeulen (Radboud University)

Motivation: We obtained our first big NWO consortium grant (NWO/PSIDER), a project I had initiated together with Michiel Vemeulen. We will develop human embryo models to study the mechanisms of implantation into the uterus and the role of chromosome copy number variations as the cause for miscarriages. For this project we will use EpiDamID (developed as described under Oncode base fund project A) to obtain single-cell epigenetic and transcriptomic measurements.

KWF research grant: €660K (awarded in 2020)

Oncode Investigator: Madelon Maurice (UMC Utrecht)

Motivation: Without Oncode support, it would have been difficult to initiate this research line as the work is entirely new to my lab and a proven track record is commonly required to acquire funding. With our preliminary findings we obtained KWF funding to continue our efforts.

Boehringer Ingelheim: €175K

Oncode Investigator: Linde Meyaard (UMC Utrecht)

Motivation: Our studies on a non-disclosed target, for which novel initiatives were previously funded by Oncode base funding, have progressed to be mainly funded by collaborative research agreements with non-private partners, including animal studies in disease models.

KWF YIG: €560K

Oncode Investigator: David Huels, (Jan Paul Medema group (Amsterdam UMC))

Motivation: The project only recently started in the lab but has already yielded important insights. Using organoid technology in different ECM matrices we reveal that regenerative populations are observed when cells are placed in collagen. The underlying mechanism is now part of the YIG project of David Huels who developed the project in my lab.

KWF research grant : €750K

Oncode Investigator: Sylvie Noordermeer (LUMC)

Motivation: This project has been funded by my Oncode base funds. The preliminary data obtained enabled us to get funding from KWF (750K) to proceed with the project for the next 4 years.

NWO Vidi: €800K

Oncode Investigator: Hugo Snippert (UMC Utrecht)

Motivation: Initiated with an Oncode base fund. I will expand its scope using a newly acquired NWO VIDI grant.

Non disclosed industry grant: €400K

Oncode Investigator: Anne Rios (PMC)

Motivation: The model has sparked the interest of a major industrial player for understanding human milk production and downstream effects on gut homeostasis, resulting in a sponsored contract for a PhD position.

KWF consortium grant: €1M (awarded in 2020)

Oncode Investigator: Anne Rios (PMC)

Motivation: Our BEHAV3D platform for accessing cellular immunotherapy efficacy and mode of action has now been rolled out over several research projects, including two funded consortia grants and a project

sponsored by a main player in the pharmaceutical industry. This will further validate the platform and especially its potential to guide and improve clinical trial design for immune-oncology drugs.

NKI foundation €3.5M

Oncode Investigator: Bas van Steensel (NKI)

Motivation: The Oncode Synergy scheme has catalysed the formation of a strong consortium of seven labs that have now started a large project (supported by external funding) to study noncoding mutations in cancer genomes

KWF research grant: €422K

Oncode Investigator: Louis Vermeulen (Amsterdam UMC)

Motivation: We found that the compound lithium has a chemopreventive effect on adenoma development in mice. We patented this finding and we recently obtained funding from the Dutch Cancer Society (KWF) to perform a clinical trial in humans with familial adenomatous polyposis.

KWF grant: €710K, **Health-Holland PPP match call:** €348K

Oncode Investigator: Louis Vermeulen (Amsterdam UMC)

Motivation: In 2021, we obtained 2 grants to be able to further study effective treatment of PMD: One KWF grant (together with Dr. Maarten Bijlsma, and Prof. Dr. Onno Kranenburg) and a TKI grant (with Dr. Maarten Bijlsma and the drug formulation company Avivia BV).

NWO research grants: €247K and €295K

Oncode Investigator: Wim Vermeulen (Erasmus MC)

Motivation: Funding *C. elegans* research is intrinsically challenging within the Dutch funding-landscape, but through base-fund enabled results we acquired two *C. elegans*-associated research grants (NWO-ENW: ALWOP.494; and 711.018.007).

Appendix III

Advice letter IAB

Date: May 16, 2022

Subject: International Advisory Board, assessment Annual progress report 2021

Annually, Oncode provides its International Advisory Board (IAB) with its annual progress report, updating the board with the Institute's overall performance of the preceding year, progression towards strategic objectives and outlook for the upcoming years. Hereupon the IAB performs a qualitative review of Oncode's performance and provides a comprehensive advice on all aspects of Oncode's performance at the institutional level. Our advice can be found below. As Oncode is entering into its next phase, this year's annual IAB meeting covered not just Oncode's progression to its strategic objectives but was also very much focussed on Oncode's future plans and activities. For this Oncode provided the IAB with the following documentation:

- Annual progress report 2021
- IRC assessment report 2022
- Strategic plan phase 2

During the subsequent video conference Oncode's Management Board (MB) presented and discussed the following topics with the IAB:

- Annual progress on basis of annual report 2021
- Oncode phase 2
 - o Strategic plan,
 - o OI assessment and selection

Both the provided materials as well as discussions the IAB had with Oncode's MB during the video conference form the basis of our advice. The combination of the annual progress report, the phase 2 strategic plan and the discussions during the videoconference provided the board with well-balanced insight into the developments and current state of affairs of the Institute.

Annual Progress:

Overall, the IAB concludes, that progress of Oncode is on track and finds its activities and achievements outstanding. To quote some IAB members: *"I have been very impressed with the overall strategy of Oncode and the performance of Oncode (at four years in) against that strategy. [...]. In my view Oncode is performing very well as 'an independent institute dedicated to both understanding cancer and also translating research into practice".* (Paul Workman) and *"Very impressed that the impact of the COVID-19 pandemic was minimal, with research activities (including clinical trials) progressing as expected!"* (Vishva Dixit).

Similarly, the IAB members are positive about the progress made within the different Key Performance Area's (KPA's). The progress made in the KPAs for scientific excellence and collaborative excellence are applauded. *"The breadth, impact, and number of papers is exceptional and internationally competitive. Equally, the Investigators continue to generate significant leveraged funds, with direct impact of Oncode funding on both papers and funding income (both public and private) becoming more apparent"*. (Richard Marais). Some IAB members caution Oncode not to put too much emphasis on high impact publications. And since Oncode has made great strides in increasing collaborations within Oncode, more emphasis should now be placed on supporting international collaborations.

Similar to previous years the IAB members conclude that although laudable progression has been made in within the KPAs for patient benefit and affordable healthcare, it is still early days to assess the long term impact of the different activities. The IAB is pleased to see that the clinical proof of concept and drug repurposing (DR) programmes are readily being used by the Oncode community and stresses the importance of maintaining focus on these types of activities in the future funding period, to ensure impact will be achieved. Paul Workman notes that caution is required with DR screens, researchers should be adequately supported by Oncode as results from DR screens can be misleading and require critical scrutiny, careful validation and in-depth follow-up.

The progress made within the KPA for valorization excellence are well on track and the IAB is particularly impressed with the leveraging of public funds by Oncode and the launch of two new Oncode spin off companies. With a growing portfolio of patents, license and equity positions, the IAB stresses that Oncode must actively manage its portfolios and ensure it can carry the financial burden involved. Furthermore, it encourages Oncode to clearly communicate its financial model to its partner institutes i.e. 'where the money comes from and where it goes'. Emplacing that Oncode is not established to generate profits, communicating to ensure its partner institutes understand this financial model is important.

During the online meeting, Oncode took the opportunity to update the board on multiple aspects of Oncode's future plans and the steps it has taken in the last year towards achieving a second 5 year term for Oncode.

Strategic plan:

In previous years multiple elements of Oncode's phase 2 plans have been discussed with the IAB, and the board is pleased to now see these plans in the final strategic plan which was provided to the board prior to the meeting.

While the plan was not discussed at length, several elements were discussed during the meeting of which the IAB would like to note the following:

- MD/PhD programme: Since the IAB has always been very vocal about the importance of integrating clinician scientists in the institute early on in their careers, it is disappointed that the programme has not been included in Oncode's phase 2 plans. The IAB urges Oncode to seek a means of financing this programme which it views as of critical importance
- Oncode Accelerator Projects (OAP): The IAB has been part of the selection of the 3 projects included in the phase 2 strategic plan and is therefore pleased to hear that already two of these

projects have received external funding. The board sees the OAPs as a natural way to promote collaboration within Oncode and in particular, also outside of Oncode

- Valorisation outside of Oncode: The success of Oncode valorization strategy is reflected by the request of stakeholders to also take on the valorization of IP from non-Oncode sources. The IAB does note that Oncode should be mindful not to stretch its resources too thinly by taking on additional work without having the proper mechanisms in place to ensure Oncode is properly compensated for its activities or these efforts are otherwise funded.
- Facilities and Infrastructure: Multiple members of the IAB have indicated the importance of access to high end facilities and infrastructure. In phase 2 these should be maintained, and it should be ensured that they deliver to the community. Since the budget for Facilities and Infrastructure is decreased in phase 2, the IAB urges Oncode to seek additional/new means to finance these activities, for instance through cost sharing with partner institutes, fee for service models or by partnering with international research organizations.

OI assessment and selection: The IAB has been part of the OI assessment and selection procedure through the assessment of the RMC members and by advising on the final conclusions made by the MB in the assessment procedure. The IAB was pleased to be updated on the final decisions made by Oncode's management after assessment of the International Review Committee (IRC). The IAB is encourage by the corrective measures which have been taken to counter gender inequality in the assessment results. The IAB made several suggestions to actively counter gender inequality more pro-actively as well as best practices in assessment and recruitment procedures.

Overall, the board is pleased with the progress reported and satisfied with the steps taken to ensure Oncode's phase 2 funding. The board is confident that Oncode will continue to make strides to generate impact for cancer patients.

Respectfully submitted,



Teri Willey (Chair), on behalf of the International Advisory Board (Dr. Vishva Dixit, Prof. Clare Isacke, Prof. Richard Marais, Prof. Alberto Bardelli, Prof. MD. Sabine Tejpar, Prof. Paul Workman)

Response Oncode

Date: May 23, 2022

Subject: Response Oncode to advise International Advisory Board

Note: Oncode's response to the IAB has been highlighted in orange

Annually, Oncode provides its International Advisory Board (IAB) with its annual progress report, updating the board with the Institute's overall performance of the preceding year, progression towards strategic objectives and outlook for the upcoming years. Hereupon the IAB performs a qualitative review of Oncode's performance and provides a comprehensive advice on all aspects of Oncode's performance at the institutional level. Our advice can be found below. As Oncode is entering into its next phase, this year's annual IAB meeting covered not just Oncode's progression to its strategic objectives but was also very much focussed on Oncode's future plans and activities. For this Oncode provided the IAB with the following documentation:

- Annual progress report 2021
- IRC assessment report 2022
- Strategic plan phase 2

During the subsequent video conference Oncode's Management Board (MB) presented and discussed the following topics with the IAB:

- Annual progress on basis of annual report 2021
- Oncode phase 2
 - o Strategic plan,
 - o OI assessment and selection

Both the provided materials as well as discussions the IAB had with Oncode's MB during the video conference form the basis of our advice. The combination of the annual progress report, the phase 2 strategic plan and the discussions during the videoconference provided the board with well-balanced insight into the developments and current state of affairs of the Institute.

Annual Progress:

Overall, the IAB concludes, that progress of Oncode is on track and finds its activities and achievements outstanding. To quote some IAB members: *"I have been very impressed with the overall strategy of Oncode and the performance of Oncode (at four years in) against that strategy. [...]. In my view Oncode is performing very well as 'an independent institute dedicated to both understanding cancer and also translating research into practice"*. (Paul Workman) and *"Very impressed that the impact of the COVID-19 pandemic was minimal, with research activities (including clinical trials) progressing as expected!"* (Vishva Dixit).

Similarly, the IAB members are positive about the progress made within the different Key Performance Area's (KPA's). The progress made in the KPAs for scientific excellence and collaborative excellence are applauded. *"The breadth, impact, and number of papers is exceptional and internationally competitive. Equally, the Investigators continue to generate significant leveraged funds, with direct impact of Oncode funding on both papers and funding income (both public and private) becoming more apparent"*. (Richard Marais). Some IAB members caution Oncode not to put too much emphasis on high impact publications. And since Oncode has made great strides in increasing collaborations within Oncode, more emphasis should now be placed on supporting international collaborations.

Oncode is pleased to learn that the IAB is positive about the progressions made with the KPA scientific excellence. Oncode agrees with the IAB that not too much emphasis should be placed on high impact publications and will take this into account for future reports. Oncode would like to stress that in its recently conducted investigator assessment, it has placed the emphasis on the narrative behind the science of investigators rather than on metric data.

Oncode is mindful that more emphasis should be placed on supporting international collaboration, it is therefore that this has also become a strong element in Oncode collaborative strategy in phase 2. Recent successes such as the pan-European public private partnership with the Innovative Medicines Initiative of the EU, the participation of European UNCAN.eu initiative as part of Europe's Beating Cancer plan and the established strategic alliance with CRUK have already increased Oncode's international visibility.

Similar to previous years the IAB members conclude that although laudable progression has been made in within the KPAs for patient benefit and affordable healthcare, it is still early days to assess the long term impact of the different activities. The IAB is pleased to see that the clinical proof of concept and drug repurposing (DR) programmes are readily being used by the Oncode community and stresses the importance of maintaining focus on these types of activities in the future funding period, to ensure impact will be achieved. Paul Workman notes that caution is required with DR screens, researchers should be adequately supported by Oncode as results from DR screens can be misleading and require critical scrutiny, careful validation and in-depth follow-up.

Oncode realizes that indeed it is still early days to assess the full impacts made within the patient benefit and the affordable healthcare KPA's. Both elements are maintained within Oncode's phase 2 strategy. Following the assessment of the phase 2 strategic plan by the International Review Committee, Oncode has made several critical changes to its strategy to ensure more emphasis is placed on achieving clinical impacts within the institute's activities.

Oncode agrees with Prof. Workman that researchers should be properly supported in relation to DR screens. It is for this reason that Oncode has installed a DR advisory board, which not only reviews screening request but also advises researchers on the validation and follow up of their screens.

The progress made within the KPA for valorization excellence is well on track and the IAB is particularly impressed with the leveraging of public funds by Oncode and the launch of two new Oncode spin off companies. With a growing portfolio of patents, license and equity positions, the IAB stresses that Oncode must actively manage its portfolios and ensure it can carry the financial burden involved. Furthermore, it encourages Oncode to clearly communicate its financial model to its partner institutes i.e. 'where the money comes from and where it goes'. Emplacing that Oncode is not established to generate profits, communicating to ensure its partner institutes understand this financial model is important.

Oncode recognizes that with its growing IP, license and equity portfolios resources required to maintaining and managing such portfolios inherently increase as well. Oncode is restricted in costs that can be made for prosecution and maintenance of its IP portfolio beyond the national phase, which helps keeping costs under control, however, it can at the same time jeopardize IP positions if licensees are not identified quickly enough.

As part of our current activities concerning phase 2, the Affiliation Agreement Oncode has established with its partner institutes is re-negotiated. Within these discussion with Oncode's partner institutes, Oncode is always mindful to clearly reiterate the Oncode financial model.

During the online meeting, Oncode took the opportunity to update the board on multiple aspects of Oncode's future plans and the steps it has taken in the last year towards achieving a second 5 year term for Oncode.

Strategic plan:

In previous years multiple elements of Oncode's phase 2 plans have been discussed with the IAB, and the board is pleased to now see these plans in the final strategic plan which was provided to the board prior to the meeting.

While the plan was not discussed at length, several elements were discussed during the meeting of which the IAB would like to note the following:

- MD/PhD programme: Since the IAB has always been very vocal about the importance of integrating clinician scientists in the institute early on in their careers, it is disappointed that the programme has not been included in Oncode's phase 2 plans. The IAB urges Oncode to seek a means of financing this programme which it views as of critical importance
In line with the IAB, Oncode sees an MD/PhD programme as an essential element to ensure a better integration of clinical science within the institute. It will therefore seek different means to finance these activities or align with funding partners or partners institutes to set up such a programme
- Oncode Accelerator Projects (OAP): The IAB has been part of the selection of the 3 projects included in the phase 2 strategic plan and is therefore pleased to hear that already two of these projects have received external funding. The board sees the OAPs as a natural way to promote collaboration within Oncode and in particular, also outside of Oncode
- Valorisation outside of Oncode: The success of Oncode valorization strategy is reflected by the request of stakeholders to also take on the valorization of IP from non-Oncode sources. The IAB does note that Oncode should be mindful not to stretch its resources too thinly by taking on additional work without having the proper mechanisms in place to ensure Oncode is properly compensated for its activities, or these efforts are otherwise funded.
Oncode realizes that the proposed activities can only be provided if additional resources can be secured. Moreover, Oncode also would like to stress that the proposed valorization activities outside of Oncode will only be provided to stringently selected research projects of high quality.
- Facilities and Infrastructure: Multiple members of the IAB have indicated the importance of access to high end facilities and infrastructure. In phase 2 these should be maintained, and it should be ensured that they deliver to the community. Since the budget for Facilities and Infrastructure is decreased in phase 2, the IAB urges Oncode to seek additional/new means to finance these activities, for instance through cost sharing with partner institutes, fee for service models or by partnering with international research organizations.
Oncode shares the board's vision on the importance of high-quality facilities and infrastructures. While indeed the current phase 2 budgets for these activities are decreased, Oncode sees multiple opportunities to seek external leveraging funds to maintain and renew its facilities and infrastructure.

OI assessment and selection: The IAB has been part of the OI assessment and selection procedure through the assessment of the RMC members and by advising on the final conclusions made by the MB in the assessment procedure. The IAB was pleased to be updated on the final decisions made by Oncode's management after assessment of the International Review Committee (IRC). The IAB is encouraged by the corrective measures which have been taken to counter gender inequality in the assessment results. The IAB made several suggestions to actively counter gender inequality more pro-actively as well as best practices in assessment and recruitment procedures.

Oncode valued the contribution of the IAB to the selection procedure. Oncode expects that several of the suggestions made by the IAB will already be implemented in its upcoming assessment and recruitment procedures. Oncode will contact individual IAB members to learn from best practices.

Overall, the board is pleased with the progress reported and satisfied with the steps taken to ensure Oncode's phase 2 funding. The board is confident that Oncode will continue to make strides to generate impact for cancer patients.

Respectfully submitted,

A handwritten signature in cursive script, reading "Teri Willey".

Teri Willey (Chair), on behalf of the International Advisory Board (Dr. Vishva Dixit, Prof. Clare Isacke, Prof. Richard Marais, Prof. Alberto Bardelli, Prof. MD. Sabine Tejpar, Prof. Paul Workman)

Appendix IV

Oncode Investigator Research Summaries

Will be provided separately.