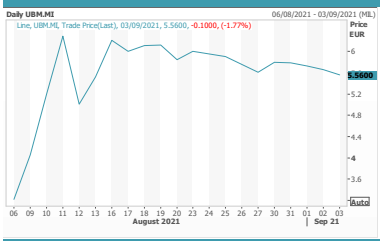
Healthcare



Source: Refinitiv

Market data

EPIC/TKR	**UBM.MI**
Price (€)	**5.58**
12m high (€)	7.55
12m low (€)	3.00
Shares (m)	7.25
Mkt cap (€m)	45
EV (€m)	39
Free float*	31.8%
Country of listing	Italy
Market	AIM

*As defined by AIM Rule 26

Description

Ulisse BioMed has developed diagnostic platforms that have wide applications in molecular and immunoassay. It is currently selling tests for HPV and coronavirus, and has a strong development pipeline.

Company information

Chairman	Saverio Scelzo
CEO	Matteo Petti
COO	Bruna Marini
CSO	Rudy Ippodrino

+39 040 3757540
www.ulissebiomed.com

Key shareholders

Rudy Ippodrino	5.8%
Bruna Marini	3.9%
Copernico Innovazione	11.7%
1,153 others subject to lock-up	46.8%

Diary

Sep'21	Interim results
Mar'22	Final results

Analyst

Jason Streets 020 3693 7075
js@hardmanandco.com

ULISSE BIOMED

Molecular diagnostic game changer

Ulisse BioMed (UBM) has developed three technology platforms that offer great potential, having wide applications in molecular diagnostics and immunoassay. Its most developed product – a polymerase chain reaction (PCR) test for coronavirus – is already being manufactured, with other diagnostic tests following shortly on the same platform. Two other technologies involve nanoswitches and aptamers; these have great potential, but they will be developed further in the future. We forecast UBM to be continuously EBITDA-positive from 2021 onwards. Following the successful IPO, it has a strong balance sheet.

- **Revenues:** UBM's molecular diagnostic coronavirus test, CoronaMelt, has several advantages over other tests, being more sensitive and more accurate, and it can work without the purification step, making it faster and cheaper too. UBM has signed an agreement with a large Italian firm, Menarini, to commercialise this and future viral respiratory disease tests.

- **Future:** UBM has also developed tests for HPV and some STDs. These are currently for research use only ("RUO"). It has further created a diagnostic platform, using nanoswitches, which outperforms the current gold standard test for monitoring biological drugs, helping to reduce both side effects and drug costs.

- **Valuation:** Valuing such early-stage businesses is extremely difficult. We have used both a DCF model and comparable company EV/revenue analysis. The DCF derives an equity market value of €42m to €53m, or €5.17 to €6.56 per share, and the peer comparable value is €56m, or €6.87 per share.

- **Risks:** While diagnostic tools do not have to follow the same stringent trials as new drugs, they still require approval, and only a few of UBM's products are approved for commercial usage in the EU. Other products require both further successful development and commercial partners; neither is guaranteed.

- **Investment summary:** UBM has developed three separate technology platforms, addressing three large and fast-growing markets. It has also developed some products on these platforms, mostly in the field of diagnostics, which have superior characteristics – speed, accuracy, simplicity – to the current solutions. Having raised €5m in a successful IPO on AIM Italia, UBM is well-placed to commercialise them and fund the ongoing development of new solutions.

Financial summary and valuation

Year-end Dec (€000)	2019	2020	2021E	2022E	2023E	2024E
Product sales	11	129	60	700	1,400	2,100
Royalties	0	0	110	900	1,500	2,500
Collaboration revenues	0	300	280	600	130	0
Total revenues	399	763	550	2,540	3,210	4,730
EBITDA	-1,043	275	95	1,585	2,000	3,360
EBIT	-1,099	224	-150	1,250	1,500	3,100
Net profit (loss)	-1,098	222	-120	1,200	1,400	2,350
EPS (fully diluted, €)	nm	nm	nm	0.12	0.14	0.24
Net (debt)/cash	776	43	6,206	6,606	8,106	10,206
Shares issued (m)		5.0	6.0	8.1	8.1	8.1
P/E (x)				45.2	38.7	23.1
EV/sales (x)			50.0	15.2	11.6	7.4

Source: Hardman & Co Research

Table of contents

The company

Operates in three specific segments of biotech market

UBM operates in three specific segments of the biotech market: molecular diagnostics (Sagitta), theranostics (Nanohybrid), and, looking out further, the field of therapeutics and medical devices based on aptamers (Aptavir). Its most developed is molecular diagnostics.

UBM is aiming to make advanced diagnostics and personalised medicine an everyday reality, supporting the identification of potential diseases in a quick and cheap way, helping take the right measures in time, and monitoring the impact of treatment and its effectiveness.

UBM believes that the best way to do this is by applying innovative solutions in the field of *in-vitro*[1] diagnostics (IVD), in particular focusing on molecular diagnostics. Designing and developing drugs may be the glamourous side of the healthcare industry, but diagnostics starts before the patient is even a patient, and continues right through to treatment and aftercare.

Sagitta

Single-channel capability…

Sagitta is UBM's platform for molecular diagnostics ("MDx"), which serves as the backbone for its core MDx products: assays – non-reusable tests for disease detection – that can be analysed using existing RT-PCR machines already in common use.

Sagitta's proprietary chemistry is based on a specific saturating dye-based formula that can identify and discriminate up to 20 targets in a single reaction, using only a single-channel, real-time PCR. Sagitta tests have high sensitivity (up to 20 molecules per reaction). The high sensitivity is the ability to detect the target, starting from a lower number of target molecules. The sensitivity is related to the limit of detection ("LoD"): the minimum number of target molecules needed to be able to give a positive result. A lower LoD means higher sensitivity. A higher sensitivity could imply a lower specificity (i.e. accuracy), but Sagitta maintains a high specificity, thanks to the melting curve analysis.

…very efficient in terms of time and cost

The single-channel capability means it can be used in any PCR machine, and the high multiplexing means it is suitable for syndromic testing. Syndromic testing is when you do one test for multiple pathogens at the same time that share the same symptoms, rather than multiple tests: one for each pathogen. This is much more efficient, in both time and cost.

Further efficiency is derived from the Sagitta assays not requiring expensive and time-consuming purification steps. By using UlisseFaster, a reagent developed by UBM, the raw biological sample is suitable for use in a PT-PCR machine, which laboratories can process quickly. If necessary, it is possible to order a customised liquid-handling robotic system to automate the UlisseFaster treatment process. Management estimates that the savings can range between €3 and €8 per test.

Sagitta works with a wide range of biological samples, making their collection easier and suitable for self-collection. It can perform analysis on any body fluid: saliva, sputum, vaginal secretion, blood serum and urine.

Sagitta is particularly suitable for detecting and discriminating among nucleic acid mutations. It has recently been applied to detecting SARS-CoV-2 variants.

[1] *In vitro* means, literally, in glass, e.g. in a test tube or petri dish, and is used as opposed to *in vivo*, i.e. in the body.

Very well-placed to exploit PCR testing opportunity

We are all too familiar with PCR testing for COVID-19, and how long the requirement for this pandemic testing continues remains unknown, but the widespread installation and use of PCR machines means that there is a ready market for future use to detect and diagnose different diseases. And Sagitta, with its advanced multiplexing capabilities, which are crucial for syndromic testing, is extremely well-placed to exploit this opportunity.

Products

UBM has developed eight molecular assays, three commercial and five currently for RUO, and one reagent (currently research only, but pending CE-IVD approval). All of them are designed for use in standard RT-PCR machines.

LadyMed and HPV Selfy

LadyMed and HPV Selfy able to detect 14 different HPV strains

LadyMed and HPV Selfy are the first, highly innovative, products originated on the Sagitta platform. They are RT-PCR tests for Human Papillomavirus ("HPV"), which is responsible for cervical cancer. HPV is a very common virus, which affects about 10% of women. On average, every female is infected at least once by HPV during her lifetime.

The tests are able to detect 14 different HPV strains – responsible for 96% of cervical cancer – with a single reaction, on an unpurified self-collected sample. LadyMed is a retail version – purchasable and usable directly by the patient – and HPV Selfy is for use in a laboratory. The genotyping capability of the test is a critical aspect of the diagnostic process, and new cervical screening programmes are focused on genotyping. The global cervical cancer diagnostic market was worth €7.8bn in 2020.

LadyMed has CE-IVD approval, which means it can be legally commercialised within the EU.

CoronaMelt and CoronaMelt Var

CoronaMelt and CoronaMelt Var are highly accurate molecular tests

The second group of products is CoronaMelt and CoronaMelt Var, both also marked CE-IVD. CoronaMelt is a diagnostic test for SARS-CoV-2. It is a molecular test, belonging to the category NAAT (nucleic acid amplification test), which is recommended by the FDA.

CoronaMelt can analyse saliva and nasal samples and, if used with the reagent UlisseFaster, without the nucleic acid purification step. Molecular tests are much more accurate than the antigen tests we have all got used to.

UBM believes its product is superior to most molecular tests in the market. It provides specific viral melting curves, coupled with amplification curves, generating a unique SARS-CoV-2 melting fingerprint profile. This increases the test sensitivity and its specificity, reducing both false positives and false negatives. In addition, thanks to the native genotyping granted by the melting curve analysis, CoronaMelt is able to detect and genotype in a single diagnostic process.

The current global COVID-19 pandemic has demonstrated the potential huge cost of both false positives and false negatives.

CoronaMelt comparable performance

FEATURE	CORONAMELT	OTHER RT-PCR TESTS	NOTES
AVERAGE SENSITIVITY	>95%	81-88%	According to several metanalysis the average sensitivity of RT-PCR Sars-CoV-2 tests is low. CoronaMelt is one of the most sensitive test available on the market.
AVERAGE SPECIFITY	>99%	<99%	Melting temperature profile allows to be sure that the detected amplicons are Sars-CoV-2 amplicons. No test on the market is providing this result.
NO EXTRACTION	YES	VERY FEW	Easier and faster workflow with less workforce, reagents and equipment, using a CE-IVD solution: costs and time saving, granting reliability.
VARIANT GENOTYPING IN A SINGLE STEP	YES	NO	Most diffused variant genomes detection in the same CE-IVD reaction, without need of further sequencing or second reflex tests. Can be easily updated when new variants pop out.
VALIDATED ON SALIVA	YES	VERY FEW	CoronaMelt is one of the few tests clinically validated on saliva.

Source: UBM

An independent study by Centro Diagnostico Italiano compared CoronaMelt's efficacy with the Pelkin Elmer test. The Pelkin Elmer test had performed well in an FDA study, when it had the lowest limit of detection LoD among 195 different tests. LoD is a measure of sensitivity – how many molecules of viral material in a given sample do there need to be for the test to turn positive?

For a given amount of viral material, there will need to be a number of RNA amplification cycles before it can be detected. The fewer cycles needed, the more sensitive is the test. Fewer cycles are good, because this is more likely to avoid false negatives. CoronaMelt achieved the same LoD as Perkin Elmer at least three or four amplification cycles earlier. CoronaMelt is more sensitive and, thanks to the melting signature, it is able to distinguish between low copy number amplicons and aspecific signals.

CoronaMelt Var detects SARS-CoV-2 variants. It has CE-IVD approval, so can be used as a tier 1 test for screening purposes. Most competing tests are for RUO, and can only be used as a Tier 2 test for genotyping after a positive COVID-19 test.

Menarini Diagnostics

First commercial partnership

UBM entered into an agreement with Menarini Diagnostics for the production and commercialisation of CoronaMelt and CoronaMelt Var. Menarini is the largest pharma company in Italy by turnover. The agreement already includes new COVID-19 variants and other diseases of the respiratory viral panel. Menarini will request the development of these new tests and pay for the development costs. While there is some variation among panels, most multiplex PCR-based respiratory viral panels test for influenza, respiratory syncytial virus (RSV), adenovirus, parainfluenza virus, adenovirus, coronavirus, rhinovirus, enterovirus and human metapneumovirus; some also include bocavirus, and offer subtyping of influenza, parainfluenza, RSV and coronavirus.

Menarini Diagnostics started production of CoronaMelt and launched the commercial product in April 2021. CoronaMelt Var should follow in September 2021.

UlisseFaster

Ulisse-Faster works in way that reduces costs, workflow and time

UlisseFaster is a reagent developed by UBM for the pre-treatment of biological samples, which avoids the phase related to the extraction and purification of DNA/RNA – thus saving costs, and reducing workflow and time required.

Menarini Diagnostics has set up a facility for the production of MDx reagents with a production capacity of 300,000 tests per month. The production capability can be easily doubled by organising the workflow over two shifts (now based on a single shift), and could be further increased to up to two million tests per month, introducing a robotic handling system.

Other products

Other products are RUO

The other Sagitta products are currently classified as RUO. They include:

- Sexually transmitted diseases: Chlamydia + Gonorrhoea, Syphilis and other HPV types. At the moment, UBM has developed an assay for the concurrent detection of Chlamydia and Gonorrhoea, and one for identification of Syphilis.

In addition, UBM has come up with two additional HPV diagnostic tests ("low-risk" HPV and "probably high-risk" HPV).

- HPV for oropharyngeal cancer, a diagnostic test that allows the detection and genotyping of high-risk HPV present in paraffin-embedded samples of oropharyngeal cancer and in biopsies.

Other projects

UBM also has some projects that are yet to be initiated on the Sagitta platform, covering pneumonia, herpes and sepsis, in addition to cancers other than that related to HPV: colon, melanoma and lung cancer.

Nanohybrid

UBM's most innovative and advanced proprietary platform

Nanohybrid represents UBM's most innovative and advanced proprietary platform. It operates in the field of theranostics – a portmanteau word to describe the overlapping fields of therapy and diagnostics. The product will improve patient treatment with biological drugs by minimising over- and under-dosage. The rapid testing system will enable doctors to administer correct dosages – appropriate for each individual patient. Finessing the dosage saves money and minimises the side effects.

Biologic drugs are very expensive and are used to treat very serious illnesses, such as cancer, autoimmune, cardiovascular and neurologic diseases. The amount of drug in the patient's blood can vary enormously – up to hundred-fold – using standard doses. The drugs tend to have serious side effects – so monitoring the impact of the dosage being used and then flexing it to achieve the maximum efficacy with the lowest possible dose reduces both the cost and the harmful side effects.

Biological drugs – costs and side effects

Drug	Price	Side Effect
TYSABRI (natalizumab)	€24,000/year	PML
Herceptin trastuzumab	€29,000/year	Cardiotoxicity
Remicade INFLIXIMAB	€22,000/year	Infection
MabThera Rituximab	€15,000/year	Infection

Source: UBM

A technology that can produce fast results

UBM leverages proprietary Nanohybrid technology to replace (and improve on) the current processes. The gold standard in this field is ELISA (Enzyme Linked Immuno-Sorbent Assay). ELISA is an immunological test, which is very sensitive and used to detect and quantify antibodies, antigens, proteins, glycoproteins and hormones. The system complexes antibodies and antigens to yield a measurable result. It is a complicated, multi-step technique, which takes between two and three hours, and can only be completed in a laboratory. Nanohybrid technology can produce the same result within one to five minutes.

It is also available as a laboratory test or as a Point-of-Care ("POC") test in a cartridge, like the COVID-19 lateral flow test kits we have all been using, but with a crucial distinction: lateral flow tests are not accurate, but a Nanohybrid test can deliver the same quantitative result as ELISA through the POC format.

Nanohybrid uses molecular nanoswitches; these are very small synthetic structures capable of instantly detecting protein biomarkers directly, in complex biological matrices, from whole blood samples. (ELISA works only with blood serum – this is blood plasma from which the clotting factors have been removed.)

Nanohybrid combines the speed, ease and low cost of the lateral flow test with the sensitivity (i.e. accuracy) and quantitative aspects of ELISA. It comes in two forms: assays and a POC analysis system. The assay is in the form of a microplate homogenous assay, which can be processed using a simple chemical-clinical analyser. The assays are simple to use and easily automatable.

Nanohybrid performance comparison

Feature	NanoHybrid	ELISA	Lateral Flow
Rapid time of detection	**YES**	NO	YES
POC format	**YES**	NO	YES
Microplate format (96 samples)	**YES**	YES	NO
Quantitative analysis	**YES**	YES	NO
Raw sample analysis (whole blood)	**YES**	NO	NO
High sensitivity	**YES**	YES	NO

Method	Cost	Sensitivity	Speed	Sample
NanoHYBRID	$	+++	+++	Whole blood
SPR	$$$	++	--	Pure
ELISA	$	+++	+	Serum
Lateral Flow	$	-	++	Serum
Luminex	$$$	+++	+	Serum

Source: UBM

Business model

UBM has 10-12 target assays

UBM plans to develop a range of assays to monitor the most widely used biological therapeutic drugs. It has 10-12 targets, and has already developed one for trastuzumab (Herceptin, Roche) – a monoclonal antibody used to treat stomach and breast cancer. It aims to sell its assays as a simpler, faster alternative to ELISA, but with the same accurate and quantitative results, through the distributors who already serve this target market.

It is looking to sell the POC system – a reader and disposable cartridges – to physicians and hospitals, backed by insurance companies keen to benefit from the results of improved treatment and lower (expensive) drug wastage. It has a prototype of the reader, and it has a first test (for trastuzumab) ready. It needs to find a partner for the further development of the POC system.

In the short term, UBM needs to gain clinical validation for the 10-12 new biologicals it is developing. In the medium term, this should lead to drug monitoring assays, to be used in centralised laboratories and, in the longer term, for POC tests to be used in hospital settings.

Aptavir

An effective and cheaper alternative technology to use of monoclonal antibodies in therapeutics

Aptavir is UBM's proprietary platform for using aptamers in medical devices. It is the least well-developed of its three business strands. The technology is an effective and cheaper alternative to the use of monoclonal antibodies in therapeutics, and it is an innovative diagnostic tool.

Aptamers are nucleic acid ligands, and are one of only a few classes of molecules that can selectively bind to a specific target, including proteins, peptides, carbohydrates, small molecules, toxins and even live cells. They are anti-viral molecules. They assume a variety of shapes, due to their tendency to form helixes and single stranded loops. They are extremely versatile, and bind targets with high selectivity and specificity.

Target recognition and binding involves three-dimensional, shape-dependent interactions, as well as hydrophobic interactions, base-stacking and intercalation. Aptamers bind because they "fit" their targets[2].

Aptamers with an affinity for a desired target are selected from a large oligonucleotide library through a process called SELEX – Sequential Evolution of Ligands by Exponential Enrichment. Through an iterative process, non-binding aptamers are discarded, and aptamers binding to the proposed target are expanded. Initial positive selection rounds are sometimes followed by negative selection to improve the selectivity of the resulting aptamer candidates.

Multiple rounds of SELEX are performed with increasing stringency to enhance enrichment of the oligonucleotide pool.

The advantages of aptamers are that they can be developed against molecules 10 times smaller than the smallest antibody targets, and, because they are very small, they are efficient at penetrating tissues to reach specific targets. They should also be cheaper to manufacture: once the optimal aptamer sequences have been selected, the production of new batches is fast and inexpensive.

[2] The word aptamer comes from the Latin, *aptare*, to fit.

They have a further advantage: because no organisms are involved in the production process, regulatory procedures are reduced compared with animal-based or cell-based production.

Products

Potentially two new products to be developed using this technology

UBM is looking to develop two sorts of products using this technology: aptamers for therapeutic purposes, and additives for pharmaceutical preparations and medical devices. It has developed some aptamers that can be used for both therapy and prevention of HPV infections (both genital and cutaneous), and it can use the same technological platform to generate more aptamers capable of inhibiting the infection of other viral pathogens.

Furthermore, it can develop aptamers for adding to pharmaceutical preparations and medical devices. These can be used in skin creams and lotions for mucous membranes, topical creams and genital gels, and even in condom lubricants, in order to enhance their ability to prevent or treat disease.

This is a longer-term project for UBM, and has no revenues in our forecast period.

Market opportunity

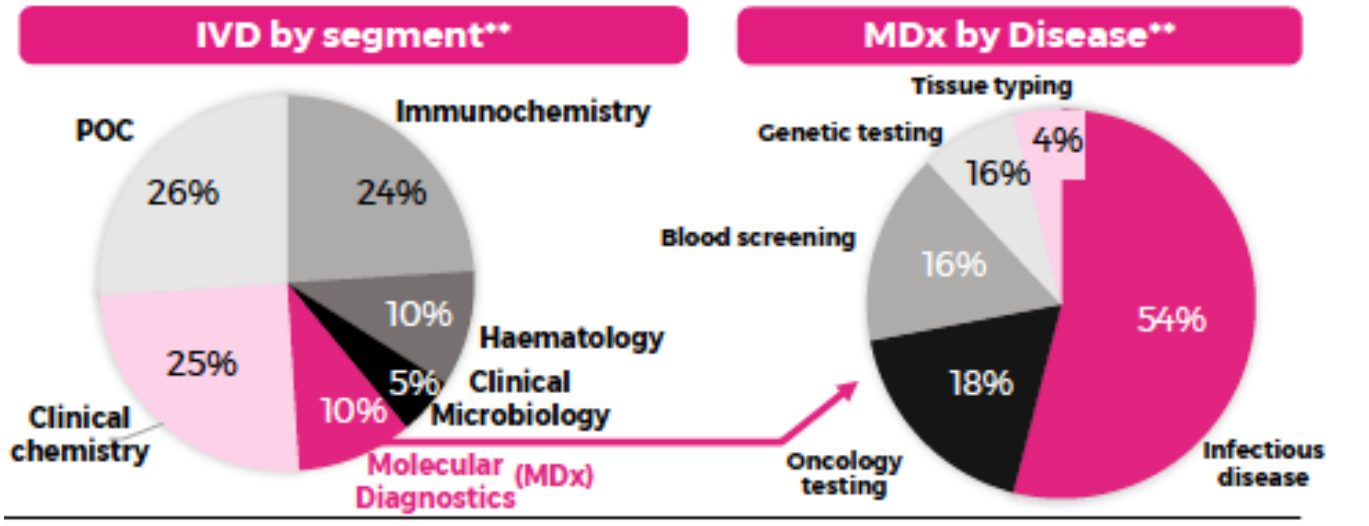
Global IVD market projected to reach $96bn by 2025, from $84.5bn in 2020 –CAGR of 2.6%

In modern healthcare, diagnostics go far beyond helping to inform a doctor whether a patient has a certain disease. Today, they are an integral part of decision-making across the entire spectrum of patient health. They enable healthcare professionals to design screening and prevention programmes. They help doctors to identify disease and define the best therapies, and they can help monitor treatment and, ultimately, the patient's recovery.

IVD products include reagents, instruments, accessories, software and controls. IVD tests are usually performed in laboratories (private or public) by trained and qualified staff with sophisticated instruments. More recently, POC testing has been developed involving testing outside the laboratory, typically in a hospital or clinic, but also at home.

The global IVD market size is projected to reach $96bn by 2025, from $84.5bn in 2020 – a CAGR of 2.6% (source: Market and Markets 2020). The rising demand for POC IVD devices has spurred the growth of the global IVD market.

IVD market and MDx within that



Source: The molecular diagnostic market, Visiongain 2017

Molecular diagnostic market

Global MDx market projected to reach $32bn by 2026, from $18bn in 2021– CAGR of 12%.

The increasing prevalence of infectious diseases, such as influenza, HPV, hepatitis, HIV and, above all, the recent COVID-19 pandemic, is pushing the development of new technologies able to detect infections and diseases like cancer, in a quick and effective manner.

Molecular diagnosis responds perfectly to this need and, for this reason, it is expected to be the fastest-growing segment of IVDs. According to research institute Markets and Markets, the global MDx market is projected to reach $32bn by 2026, from $18bn in 2021 – a CAGR of 12%.

The drivers of this growth are mainly i) increasing prevalence of infectious diseases and cancer, ii) the rising funding for R&D, and iii) the increase in POC testing devices and technological advancements.

The PCR market

PCR market valued at $4.5bn in 2019, and expected to register CAGR of 17.5%, to $8.4bn, by 2027

PCR is a ubiquitous laboratory technique used to make multiple copies of a segment of DNA. PCR is very precise, and can be used to amplify, or copy, a specific DNA target from a mixture of DNA molecules.

PCR is used in many research labs, and it also has practical applications in forensics, genetic testing and diagnostics. For instance, PCR is used to amplify genes associated with genetic disorders from the DNA of patients (or from foetal DNA, in the case of pre-natal testing). PCR can also be used to test for a bacterium or DNA virus in a patient's body: if the pathogen is present, it may be possible to amplify regions of its DNA from a blood or tissue sample.

The PCR process involves heating (denaturation), cooling (annealing) and then reheating (extension). The process is repeated many times, with the newly synthesised DNA segments serving as templates for the succeeding cycle, and hundreds of millions of copies can be created in minutes.

In 2020, the PCR segment was estimated to account for the largest share of the MDx market, by technology. According to research institute Grand View Research, the global PCR market was valued at $4.5bn in 2019, and is expected to register a CAGR of 17.5%, to $8.4bn, by 2027.

One of the major factors driving the market is the increasing demand for advanced diagnostic techniques and non-invasive pre-natal genetic testing procedures (NIPT); another factor is the rising number of Contract Research Organisations ("CRO") and forensic and research laboratories, owing to the accuracy, automation, precision, real-time quantification and sensitivity achieved.

In addition, the increased availability of government funding for conducting research based on genomics is anticipated to accelerate market growth, together with the launch of novel technologies.

Therapeutic drug monitoring market

Global TDM market projected to reach $2.0bn by 2025, from $1.4bn in 2020 – CAGR of 6.9%.

Therapeutic drug monitoring (TDM) is the clinical practice of measuring specific drugs at designated intervals to maintain a constant concentration in a patient's bloodstream, thereby optimising individual dosage regimens.

TDM is used mainly for:

- monitoring drugs with narrow therapeutic ranges;
- drugs with marked pharmacokinetic variability;
- medications for which target concentrations are difficult to monitor; and
- drugs known to cause therapeutic and adverse effects.

The process of TDM is predicated on the assumption that there is a definable relationship between dose and plasma or blood drug concentration, and between concentration and therapeutic effect.

TDM begins when the drug is first prescribed, and involves determining an initial dosage regimen appropriate for the clinical condition and such patient characteristics as age, weight, organ function and concomitant drug therapy. The goal of TDM is to use appropriate concentrations of difficult-to-manage medications to optimise clinical outcomes in patients in various clinical situations.

The global TDM market is projected to reach $2.0bn by 2025, from $1.4bn in 2020 – a CAGR of 6.9% (source: Markets and Markets 2020)

The projected growth in the market can be attributed to:

- the rise in the number of organ transplants, and the use of TDM across various therapeutic applications;
- the adoption of precision medicine; and
- the growing focus on R&D investments.

The emerging economies, such as India and China, are expected to provide a wide range of growth opportunities, driven by the rise in the cases of chronic diseases, such as cancer, in these countries.

The anti-viral therapeutics (AVT) market

Global AVT market valued at $51bn in 2020, and expected to reach $68bn in 2026 – CAGR of 5%

Anti-viral drugs are a class of medication used for treating viral infections. Most anti-virals target specific viruses, while a broad spectrum of anti-viral drugs can be effective against a wide range of viruses. Unlike most antibiotics, anti-viral drugs do not destroy their target pathogen; instead, they inhibit its development.

The general idea behind modern anti-viral drug design is to identify viral proteins, or parts of proteins, that can be disabled. These "targets" should be as little as possible like any proteins in humans, in order to reduce the likelihood of side effects. They should also be common across many strains of a virus, so that a single drug will have broad effectiveness.

Once targets are identified, candidate drugs can be selected, from either drugs already known or by designing a new candidate at the molecular level.

The target proteins can be manufactured in the lab for testing with candidate treatments by inserting the gene that synthesises the target protein into bacteria or other kinds of cells. The cells are then cultured for mass production of the protein, which can then be exposed to various treatment candidates and evaluated with "rapid screening" technologies.

The global AVT market was valued at $51bn in 2020, and it is expected to reach $68bn in 2026, a CAGR of 5% during the forecast period (source Mordor Intelligence 2020).The growth of the market is attributed mainly to the increasing focus on the treatment of COVID-19. Other factors driving the market growth include:

- the increasing R&D investments for antiviral drugs;
- strong R&D pipelines; and
- increasing product launches.

AVTs are currently available for diseases like influenza, hepatitis C and more. There is also increasing development in molecular biology promoting drug development, and the growing adoption of nucleoside and nucleotide analogues as first-line anti-virals. Based on the current development pipeline, many small molecule-based anti-viral drugs are anticipated to receive product approvals, propelling the market growth to even higher heights.

The aptamer therapeutic market

Global size of aptamer market estimated to be worth $208m in 2020, and projected to grow to $450m by end of 2025 – CAGR of 17%

Aptamers are short, single-stranded DNA or RNA molecules with defined structures, which can specifically bind to a molecular target via three-dimensional structures. Similar to the way in which antibodies bind to antigens, aptamers specifically recognise and bind to their cognate targets.

Aptamer-based therapeutics typically exploit one of three strategies:

- an aptamer can serve as an antagonist for blocking the interaction of disease-associated targets (for example, receptor-ligand interactions);
- an aptamer can serve as an agonist for activating the function of target receptors; or
- a cell-type-specific aptamer can serve as a carrier for delivering other therapeutic agents to the target cells or tissue.

The global size of the aptamer market was estimated to be worth $461m in 2020, and is projected to grow to $1,400m by the end of 2027, a CAGR of 17%. (Source: Global Industry Analysts.)

The primary factors driving the market's growth are:

- technological advancements;
- increasing R&D investments in the pharma and biotech industries;
- low cost and high efficacy in binding to large molecules compared with antibodies; and
- the patent expiration of SELEX.

This is a much smaller market compared with the other ones described, but it is new, and is expanding rapidly. It could become very large indeed.

Financials

In 2019, UBM had revenues of €11k, from an initial commercial test of LadyMed in the B2C market. Otherwise, "revenue" up until 2020 was a mixture of R&D tax credits and research grants. In 2020, there were €128k of sales related to 25,000 tests that UBM supplied to Menarini to verify the efficacy of CoronaMelt, and a further €300k of "collaboration revenues" relating to a technology transfer of part of the Sagitta platform to Menarini for the production and marketing of CoronaMelt. Remaining revenue related to research grants and R&D credits. With expensed costs of just under €500k, there was an EBITDA surplus of €275k, and net income of €222k.

Also of interest in the 2020 accounts, UBM wrote up the value of the Sagitta DNA patent to €750k, following the agreement signed with Menarini. Cash at the year-end was down to €43k, but increased from revenue debtors early in the new year.

Forecasts

Revenues should come from forming commercial partnerships…

UBM is not a sales organisation; it is an R&D business. Revenues will come from forming commercial partnerships, of which the first is with Menarini. UBM has a licensing agreement for the sale of CoronaMelt, CoronaMelt Var and a full viral respiratory panel. We expect a further agreement related to sexually transmitted diseases, and LadyMed and HPV Selfy in particular.

…and from co-development agreements

Additional revenues should come from co-development agreements to fund the R&D costs for the Sagitta panels, to be developed from 2022 onwards.

The forecast revenues come from:

- direct product sales (the UlisseFaster reagent for use with CoronaMelt to both Menarini and directly to third parties), growing at €700k each year;
- royalties on the sale of respiratory and sexually transmitted disease assays made by partners, growing to €2.5m by 2024; and
- €730k over the next two years of collaboration revenues covering the cost of the future development of Sagitta's assays.

Nearly 80% of all revenues out to 2024 will come from the association with Menarini. This is both a strength and a weakness. The relationship is already established with Menarini, and it is a large, well-respected player in the market. On the other hand, it is not a good idea to be too dependent on just one partner. Over time, we would expect UBM to build further, profitable, commercial relationships.

COVID-19 will drive about half of the CoronaMelt-driven revenues in 2022, but this falls rapidly in 2023, and is close to zero in 2024.

Costs

Bottom line, we estimate UBM to generate cash in forecast period

The cost of sales is driven by the scaling-up of the production of the reagent. Approximately half of the R&D expenses are capitalised going forward, and are amortised over three years; and the other expenses grow to reflect the growing size of the business. Marketing expenses are minimal, as this aspect of the business is left largely to partners.

The bottom line is that we forecast UBM to generate cash in each of the forecast periods, growing notably in 2023 and 2024.

Income statement

Year-end Dec (€000)	2018	2019	2020	2021E	2022E	2023E	2024E
Product sales		11	129	60	700	1,400	2,100
Royalties				110	900	1,500	2,500
Collaboration revenues			300	280	600	130	
Other revenues	236	388	334	100	340	180	130
Total revenues	**236**	**399**	**763**	**550**	**2,540**	**3,210**	**4,730**
Cost of goods				-20	-225	-480	-800
R&D expensed				-175	-430	-330	-170
Other expenses	-2,123	-1,442	-488	-260	-300	-400	-400
Total costs	**-2,123**	**-1,442**	**-488**	**-455**	**-955**	**-1,210**	**-1,370**
EBITDA	-1,887	-1,043	275	95	1,585	2,000	3,360
Depreciation & amortisation	-46	-56	-51	-245	-335	-500	-260
EBIT	**-1,933**	**-1,099**	**224**	**-150**	**1,250**	**1,500**	**3,100**
Net financial cost	-1	0	0	0	0	0	0
PBT	**-1,933**	**-1,098**	**224**	**-150**	**1,250**	**1,500**	**3,100**
Tax			-2	30	-50	-100	-750
Net profit (loss)	**-1,933**	**-1,098**	**222**	**-120**	**1,200**	**1,400**	**2,350**
No. of shares (m)			5.0	6.0	8.1	8.1	8.1
No. of shares (fully dil., m)			5.0	6.3	9.7	9.7	9.7
EPS (fully diluted, €)	**nm**	**nm**	**nm**	**nm**	**0.12**	**0.14**	**0.24**

Source: UBM, Hardman & Co Research

Balance sheet

@31 Dec (€000)	2018	2019	2020	2021E	2022E	2023E	2024E
Intangible assets	172	17	862	1,037	1,467	1,797	1,967
Tangible assets	196	156	115	115	115	115	115
Fixed assets	**368**	**173**	**977**	**1,152**	**1,582**	**1,912**	**2,082**
Inventories	113	81	68	32	186	372	558
Debtors	608	518	779	100	200	400	600
Cash	1,341	776	43	6,206	6,606	8,106	10,206
Current assets	**2,061**	**1,374**	**890**	**6,338**	**6,992**	**8,878**	**11,364**
Total assets	2,429	1,548	1,868	7,490	8,574	10,790	13,446
Provisions	-461	-105	-11	-11	-11	-11	-11
Creditors	-202	-775	-297	-277	-161	-977	-1,283
Total liabilities	**-663**	**-880**	**-308**	**-288**	**-172**	**-988**	**-1,294**
Share capital	11	50	50	50	50	50	50
Other reserves	4,990	4,951	5,621	11,384	11,384	11,384	11,384
Retained earnings	-3,235	-4,333	-4,111	-4,231	-3,031	-1,631	719
Total	**1,766**	**668**	**1,559**	**7,202**	**8,402**	**9,802**	**12,152**

Source: Hardman & Co Research

Cashflow

Year-end Dec (€000)	2018	2019	2020	2021E	2022E	2023E	2024E
EBITDA	-1,887	-1,043	275	95	1,585	2,000	3,360
Working capital ±			-727	400	-700	-50	-400
Capex			-107	-175	-430	-330	-170
Other	36	478	-174	80	-55	-120	-690
Operating cash	-1,851	-565	-733	400	400	1,500	2,100
Investment							
Financing			0	5,763			
Net cash generated	-1,851	-565	-733	6,163	400	1,500	2,100

Source: Hardman & Co Research

In August 2021, UBM was listed on AIM Italia, and raised €5m before expenses of €0.8m. For each four new shares, there was a warrant attached that could convert before the year-end at a maximum of €2.50 per share, yielding an additional €1.6m proceeds. We have assumed all these warrants are exercised.

In addition, there are a further 1.59m five-year warrants, with a maximum exercise price of €2.80. At this stage, we have not assumed that these additional warrants will be exercised, and we have not included them in our valuation calculations.

Valuation

DCF valuation gives central equity market value of €47m, or €5.83 per share, but within very wide range of €22m to €72m

Valuing such an early-stage business is fraught with difficulty. Our forecasts do not include anything for the third leg of the business, the aptamer therapeutics. They also make assumptions about future sales, and are cast in the face of the ongoing COVID-19 pandemic, whose impact on the continuing demand for coronavirus tests is unknowable.

With those caveats in mind, we have made a straightforward three-stage DCF model. The first stage is our own forecasts of net cashflow, the second stage assumes a growth rate for a four-year period, and the third stage is the perpetuity calculation. The answer is highly sensitive to assumptions on each of these growth rates, and the discount rate applied too. For these reasons, especially on such an early-stage business as this, we see the DCF more as a check for the assumed underlying growth rates, and a discount rate applied to arrive at a particular value, rather than as a driver of that value.

We have used a fixed 4% growth in perpetuity rate to reflect nominal growth in a sector that is likely to outperform GDP as a whole for the foreseeable future.

DCF valuation

€m	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
EBITDA	0.1	1.6	2.0	3.4				
Working capital ±	0.4	-0.7	-0.1	-0.4				
Capex	-0.2	-0.4	-0.3	-0.2				
Other	0.1	-0.1	-0.1	-0.7				
Operating cash	0.4	0.4	1.5	2.1	2.6	3.3	4.1	5.1
Discount factor	1.0	1.1	1.3	1.4	1.6	1.8	2.0	2.2
Discounted cash	0.4	0.4	1.2	1.5	1.7	1.9	2.1	2.3

Source: Hardman & Co Research

DCF summation

Value components	€m
2021-24E	3
2025E-28E	8
2029 onwards	30
Total	**41**
-plus net cash end-2021E	6
Equity value	47
Equity value per share (€)	5.83

Source: Hardman & Co Research

Using a 12% discount rate and a 25% mid-term growth rate, we derive a value of €47m, including the cash raised at IPO. This equates to €5.83 per share.

In the table below, we look at the impact of choosing different mid-term growth rates and different discount rates. The value varies from €22m, using a 20% discount rate and only a 20% growth rate to, at the other extreme, €72m, using a 10% discount rate and a 30% mid-term growth rate.

DCF sensitivity table @ 4% perpetuity growth

Discount rate	10%	12%	15%	20%
Mid-term growth rate	€m	€m	€m	€m
20%	56.0	42.0	30.7	21.6
25%	63.8	47.3	34.1	23.5
30%	72.5	53.3	38.0	25.6

Source: Hardman & Co Research

If we focus on our preferred 12% discount rate, the range is more a tightly defined €42m to €53m, or €5.17 to €6.56 per share.

Focusing on a 12% discount rate gives tighter DCF valuation range of €42m to €53m, or €5.17 to €6.56 per share

To illustrate the sensitivity of the perpetuity growth rate, we show, in the table below, the values if we were to use 3% instead. As can be seen, the impact is not dramatic – between 11% and 2%, especially at the lower end, where a higher discount rate is used.

DCF sensitivity table @ 3% perpetuity growth

Discount rate	10%	12%	15%	20%
Mid-term growth rate	€m	€m	€m	€m
20%	50.1	38.9	29.3	21.0
25%	56.9	43.7	32.4	22.9
30%	64.4	49.1	36.0	24.9

Source: Hardman & Co Research

Another methodology is to look at comparable company analysis. The problem here is that, while there are many listed biotech stocks and lots of diagnostic plays, many of them have either no meaningful revenues or no forecasts. With the larger players, where there are revenues and forecasts, the growth profile is completely different.

Peer group valuation in local currency

	Price	Enterprise value (m)	Revenue 2021E (m)	Revenue 2022E (m)	Revenue 2023E (m)	EV/Rev. 2021E	EV/Rev. 2022E	EV/Rev. 2023E
SenzaGen AB (SEK)	22.0	1,296	32	101	202	40.5	12.8	6.4
Genedrive PLC (GBP)	44.5	25	4	7	9	6.3	3.6	2.8
Epigenomics (EUR)	1.1	7	1	1	1	11.8	10.3	9.1
Biovica Intl (SEK)	21.9	1,335	2	39	67		34.2	19.9
Attana (SEK)	1.4	273	14	17	20	19.5	16.1	13.7
Average						19.5	15.4	10.4
Value of average applied to UBM (EUR, m)			0.6	2.5	3.2	50	49	49

Source: Refinitiv, Hardman & Co Research

Peer group valuation gives central value of €6.87 per share – higher than the DCF valuation

Here, remarkably, applying the average to each of our three years of forecasts derives nearly the same answer: an enterprise value of ca.€50m, or an equity value of €56m, equivalent to €6.87 per share. This is not too dissimilar from the top end of the range of our DCF-derived value of €6.56 per share.

The impact of including the 1.59 million additional warrants would be to dilute the value per share to €6.20.

It is only reasonable to point out that these valuations contain a substantial portion of hope and faith. The company is still in its very early stages, and much has to go right to achieve these forecasts; nor are they the limit on what can be achieved, but there are substantial risks involved.

Risks

Many risks facing UBM

UBM faces a myriad of risks. It is a very small, young business, operating in a highly competitive field, and right at the cutting edge of technology. There can be no certainty that its developed products succeed in the market place, nor that it can develop future products successfully.

Healthcare is a highly regulated sector and, while diagnostic tests are not as controlled as drugs, new products still need authorisation before they can be sold commercially, and that process can be lengthy and expensive, with no guarantee of success.

UBM has signed a licensing agreement with Menarini, and will be heavily dependent on it for the next few years. In particular, in the immediate future, it will be sales of CoronaMelt and the associated reagent, UlisseFaster, that from the bulk of the forecast revenues. The profile of the COVID-19 market for PCR tests is highly uncertain, and could end sooner than we are anticipating. We have it close to zero in 2024, but it may reduce faster than that.

The Nanohybrid technology is very advanced, and has enormous potential, but UBM still has to find a commercialisation partner for both the assays and the POC products. It also still needs to develop a test menu of the most widely used biological therapeutic drugs. In addition, the POC systems will require hardware development (probably with a partner).

If there are delays in development and revenues, then the company is likely to require additional capital in the future. The successful IPO has given it a large cushion – €5m before expenses – so this should not be an issue for some time, if ever.

There are also some more prosaic market risks. In particular, with a market capitalisation of €47m and a free float of 32%, the liquidity in the shares is likely to be poor.

Management

Matteo Petti – CEO

An experienced manager and investment banking professional, with over 15 years of experience, with a focus on M&A and listings. He has managed over 20 IPOs and listings on exchange regulated markets throughout Europe, and has covered the role of CFO and Investor Relations for several companies. He has a strong background in strategic and financial analysis, along with equity and debt fundraising.

Bruna Marini – Co-founder, Executive Director and COO

Bruna Marini got her PhD in Molecular Biology at the Scuola Normale Superiore (Pisa) for her research, performed in the Molecular Medicine Lab in ICGEB (Trieste). Her PhD thesis, focused on the study of the influence of nuclear architecture on HIV integration, was published in the prestigious *Nature* scientific journal. After her PhD, she founded Ulisse BioMed, with Rudy Ippodrino, to start her own career in applied research; she believes that scientific discoveries need to be efficiently translated into the health and wellbeing of the people. She is currently Ulisse BioMed's project manager. She managed the HPV Selfy clinical validation and, together with Rudy Ippodrino, she successfully applied for grants worth €1.5m.

Rudy Ippodrino – Co-founder and CSO

Rudy Ippodrino has worked in the gene therapy field, and his studies have been focused on recombinant adeno-associated viral vectors and gene targeting potentiation. He obtained his PhD (Molecular Biology) at the prestigious Scuola Normale Superiore (Pisa), which ranks among the top universities worldwide. During 2011, he led a team of undergraduate students through to the final selection in the worldwide Synthetic Biology competition, IGEM, organised by the Massachusetts Institute of Technology of Boston (MIT). His creativity, combined with his vocation for biotech innovation, pushed him to found Ulisse BioMed with Dr. Bruna Marini, in order to generate high-tech platforms and to develop disruptive products that can transform modern medicine. He is currently the Chief Scientific Officer of Ulisse BioMed and the main inventor of all Ulisse BioMed patents.

Luigi Colombo – Executive Director

Luigi Colombo has a degree in Chemistry and Pharmaceutical Technologies. He is adjunct professor at the Department of Drug Science, State University of Milan (Italy), and the author of several patents and publications.

He has more than 30 years' experience in R&D and operations in large pharmaceutical companies, with executive positions (Marion Merrell Dow, Hoechst Marion Roussell, Boeringer Ingelheim, Biosearch Italia, Serono, Merck Group). In 1996, he co-founded Biosearch Italia, an Italian biotech company, which he listed on the Nuovo Mercato. This company then merged with Versicor, went public on Nasdaq (changing its name to Vicuron Pharmaceuticals Inc.), and was acquired (for ca.$1.9bn) by Pfizer in 2005. Luigi left Merck, where he was VP and Managing Director, in mid-2018. He currently works as an independent consultant. He is the CEO (*pro tempore*) of SilverAid, a MedTech startup company focused on dentistry. He is also a director of the board at Nocturnal Lab SpA, a seed investment fund.

Scientific Advisory Board

Dr. Joseph Kates – Chairman

Dr. Joseph R. Kates obtained his PhD in Biochemical Sciences at Princeton University. At the age of 33, he was asked to be the founding Chairman of the Department of Microbiology in the School of Medicine at Stony Brook University, New York. Under his guidance, this department soon became a world-class centre for molecular virology.

His outstanding scientific contributions included the first demonstration that viruses code for and carry their own polymerases in the virus particle. This influenced the discovery of reverse transcriptase by Temin and Baltimore, who were awarded the Nobel Prize for this finding.

His laboratory also discovered the existence of poly-A on messenger RNA, the timing and semiconservative mode of DNA replication during meiosis – the proof that centrioles in eukaryotic cells do not arise from pre-existing centrioles, but are generated *de novo*.

After some years at Scripps Clinic, in La Jolla, as Chairman of the Department of Cellular Biology, he joined Bayer Pharmaceuticals as a Director of Research, where he was a major player in the development of recombinant Factor-VIII for the treatment of haemophilia, as well as other biotechnology product candidates. His position interacted directly with top Bayer management, and he became proficient in the strategic and tactical aspects of drug development.

He then worked as a top manager at the National Cancer Institute, where his work laid the foundation for the current designation of the site as the Frederick National Laboratory for Cancer Research. He has recently co-founded, and serves as head of, the Scientific Advisory Board of Kangti Biomedical, a company based in Singapore.

Dr. Gordon Whiteley

Dr. Gordon Whiteley spent more than 30 years in the medical diagnostics industry, directing conception, development and FDA filing of more than 75 diagnostic tests and accompanying instrumentation. This included 510(k), PMA and licensed biological filings for a variety of infectious diseases, cancer biomarkers, steroids and hormones, therapeutic drugs and cardiac markers. Prior to that, Dr. Whiteley directed the clinical lab service in microbiology for MDS Health Group Ltd.

In Toronto, Dr. Whiteley joined Leidos Biomedical Research (formerly SAIC) in 2001, to evaluate mass spectrometry as a possible diagnostic test platform. Since 2008, Dr. Whiteley has directed the Antibody Characterization Lab for the Office of Cancer Clinical Proteomics Research. Dr. Whiteley graduated from the University of Toronto with a PhD in microbiology.

Dr. Lawrence Banks

Dr. Lawrence Banks graduated from Leeds University, UK, with a BSc Honours degree in Microbiology, in 1981, and he obtained his PhD in 1984. He has a deep knowledge and substantial experience in the study of HPV.

Since 1990, he has been the Group Leader of the Tumour Virology Laboratory at ICGEB, Trieste, Italy, during which time the laboratory has become internationally renowned for its work on human papillomaviruses and their roles in the development of human malignancy.

Since 2019, Dr. Banks has been the global General Director at the ICGEB.

Prof. Robert C. Gallo

Prof. Robert C. Gallo, MD, is Co-Founder and Director of The Homer & Martha Gudelsky Family Foundation Inc, Distinguished Professor in Medicine, Institute of Human Virology at the University of Maryland School of Medicine, and Co-Founder and Scientific Director of Global Virus Network (GVN).

Dr. Gallo worked at the National Cancer Institute (NCI) for 30 years, prior to co-founding IHV in 1996. In 1976, he and his co-workers discovered interleukin-2 (IL-2), followed by the discovery of the first human retroviruses, Human T Cell Leukaemia Virus-1 (HTLV-1) and HTLV-2.

Dr. Gallo and his colleagues co-discovered HIV as the cause of AIDS, and developed the HIV blood test.

Currently, he is focusing on developing an HIV vaccine and viral oncology research.

Dr. Gallo has been awarded 35 honorary doctorates, is a member of the U.S. National Academy of Sciences and Institute of Medicine, and also a member of the National Inventors Hall of Fame.

Dr. Davide Zella

After completing his PhD and post-doctoral training, Dr. Davide Zella joined the Laboratory of Tumor Cell Biology at the National Institutes of Health in Bethesda, in Maryland, Baltimore. Subsequently, he joined the Institute of Human Virology and the School of Medicine at the University of Maryland, Baltimore.

Dr. Davide Zella has more than 25 years of experience in the field of microbiology/virology, immunology, cancer biology and molecular biology. He has produced more than 50 publications, including peer-reviewed articles and book chapters. Early in his career, Dr. Zella studied the interactions between IFN-alpha and the immuno-system, in particular the anti-proliferative ability of IFN-alpha, the regulation of chemokine receptors by Interferons, and mechanisms of intracellular replication of HIV.

More recently, the focus of Dr. Zella's research has been the study of the interaction between components of the microbiota and human cells to unveil molecular mechanisms of cellular transformation caused by bacteria. Beside the well-established association between H. pylory and gastric cancer, many reports highlight the correlation between several components of the microbiota and cancer, and, for this reason, his group is studying the link between cancerogenesis and bacteria, with particular attention on Mycoplasma.

Glossary

AVT: anti-viral therapeutics

CE_IVD: CE Marking indicates that an IVD device complies with the European In-Vitro Diagnostic Devices Directive (98/79/EC) and that the device may be legally commercialized in the EU.

CRO: Contract Research Organisations

ELISA: Enzyme Linked Immuno-Sorbent Assay

HPV: Human Papillomavirus

IVD: In Vitro Device

LoD: Limit of Detection

MDx: Molecular Diagnostics

NAAT: Nucleic Acid Amplification Test

NIPT: Non-Invasive Pre-natal genetic Testing

PCR: Polymerase Chain Reaction

POC: Point Of Care

RSV: Respiratory Syncytial Virus

RUO: Research Use Only

SELEX: Sequential Evolution of Ligands by Exponential Enrichment

STD: Sexually Transmitted Disease

TDM: Therapeutic drug monitoring

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The full detail is on page 26 of the full directive, which can be accessed here: https://ec.europa.eu/transparency/regdoc/rep/3/2016/EN/3-2016-2031-EN-F1-1.PDF

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