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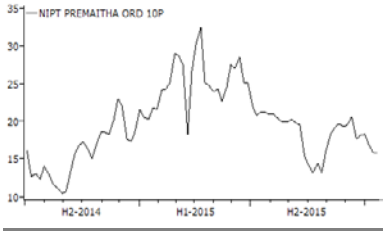
Healthcare equipment & services



Source: Fidessa

Market data	
EPIC/TKR	NIPT
Price (p)	16.0
12m High (p)	34.0
12 Low (p)	11.3
Shares (m)	228.2
Mkt Cap (£m)	36.5
EV (£m)	29.9
Free Float*	53%
Market	AIM

**As defined by AIM Rule 26*

Description

NIPT is a molecular diagnostics company using the latest DNA analysis to develop tests for non-invasive pre-natal screening. Its flagship IONA® test is the first non-invasive in vitro CE marked diagnostic for pre-natal screening to estimate the risk of a foetus having Down's syndrome or other genetic conditions.

Company information	
CEO	Stephen Little
CFO	Barry Hextall
Chairman	David Evans
	0161 667 6865
	www.premaitha.com

Key shareholders	
Concert party	39.3%
Helium	6.2%
S&W	3.9%
WB	3.3%
(Directors*	10.3%)

**Mostly included in concert party*

Next event	
Jun-16	Trading update
Sep-16	Final results

Analysts

Martin Hall 020 7148 1433
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Premaitha Health

IONA® – Up, running and available on the NHS

Premaitha uses the latest advances in DNA sequencing technology for non-invasive prenatal screening tests. IONA estimates the risk that a fetus has any of Down's, Edwards' or Patau's syndromes caused by a genetic abnormality. Although IONA is entering a competitive and litigious market, it has some advantages, is CE Marked and is the first to win a UK NHS contract. Premaitha is subject to distracting IP infringement claims but 1H'16 results showed early signs of commercial traction which are expected to accelerate herein. Also, Premaitha has signed a strategically important partnership with Thermo Fisher which adds considerable credibility.

- **Strategy:** Premaitha is using the latest DNA analysis technology for non-invasive prenatal screening (NIPT). Management is focused on the commercialisation of its flagship IONA test globally. Whilst not currently in planning or development this technology could be used for early detection of other diseases (eg cancer).

- **IONA:** This test is a screen for risk assessment that a fetus has a serious genetic disorder. The test is extremely accurate (sensitive) with few false positives and eliminates the need for unnecessary invasive follow-up tests that cause anxiety and stress. An option for sex determination has been added recently.

- **Valuation:** Similar quoted companies are more mature and have considerable sales from the US market. Companies looking for access to NGS technology have paid handsome prices, again for more mature companies. However, both these statistics augur well for Premaitha as it develops sales traction with IONA.

- **Risks:** After receiving CE Mark for IONA, Premaitha received notification that Illumina Inc had filed patent infringement claims against the company. Although Premaitha will put up a vigorous defence in the UK, litigation is an expensive, time consuming distraction and carries obvious risks if the claims are successful.

- **Investment summary:** Premaitha has an EV of £30m. The IONA test is the only product for NIPT with regulatory approval in Europe. Although the patent litigation is a distraction, commercial partnerships are being signed and these will drive future revenue growth. Our conservative assumptions, based on signed deals, still suggest that Premaitha will be EBITDA positive in fiscal 2018.

Financial summary and valuation

Year end March (£m)	2014	2015	2016E	2017E	2018E
Sales	0.00	0.00	2.50	6.21	11.61
R&D investment	-0.38	-1.85	-1.60	-1.80	-2.00
Underlying EBIT	-1.53	-4.34	-4.70	-3.40	-0.92
Reported EBIT	-1.53	-7.54	-6.72	-4.00	-1.52
Underlying PTP	-1.53	-7.45	-6.67	-4.15	-1.78
Statutory PTP	-1.53	-7.45	-6.67	-4.15	-1.78
Underlying EPS (p)	-4.13	-4.89	-3.07	-1.82	-0.78
Statutory EPS (p)	-4.13	-4.07	-2.40	-1.44	-0.62
Net (debt)/cash	-1.99	2.71	4.25	-2.19	-5.50
Shares issued	0.00	7.48	7.72	0.00	0.00
EV/sales (x)	nm	nm	nm	4.7	2.5
EV/EBITDA (x)	nm	nm	nm	-10.9	2,572.6

Source: Hardman & Co Life Sciences Research

Table of Contents

Executive summary

History

Premaitha began life as Zoragen to exploit latest DNA technology to develop a prenatal screen…

…reversed into ViaLogy and has raised £15m via Placings…

…and a further £5m (loan) as a strategic investment by Thermo Fisher

Premaitha was incorporated in 2013 for the sole purpose of acquiring the intellectual property and assets of Zoragen Biosciences LLP, a company founded in 2007 to exploit the knowledge that fetal DNA leaks into the maternal bloodstream with a view to developing an improved test (IONA) to screen for Down's Syndrome. In June 2014, Premaitha was reversed into ViaLogy plc, an AIM-listed cash shell – there is no association of Premaitha Health with the former business operations of ViaLogy. Concomitantly, new shares were issued to Premaitha Ltd shareholders as consideration for its acquisition, and a Placing & Open offer raised £7.2m to provide the working capital required to get IONA a CE Mark for commercialisation in Europe. The enlarged entity was also renamed Premaitha Health plc. In July 2015 a further oversubscribed share placing raised £8m to fund the commercialisation phase for IONA; and in December 2015 Premaitha announced a strategic investment of £5m from Thermo Fisher by way of a loan facility and corresponding issue of warrants.

The IONA® test

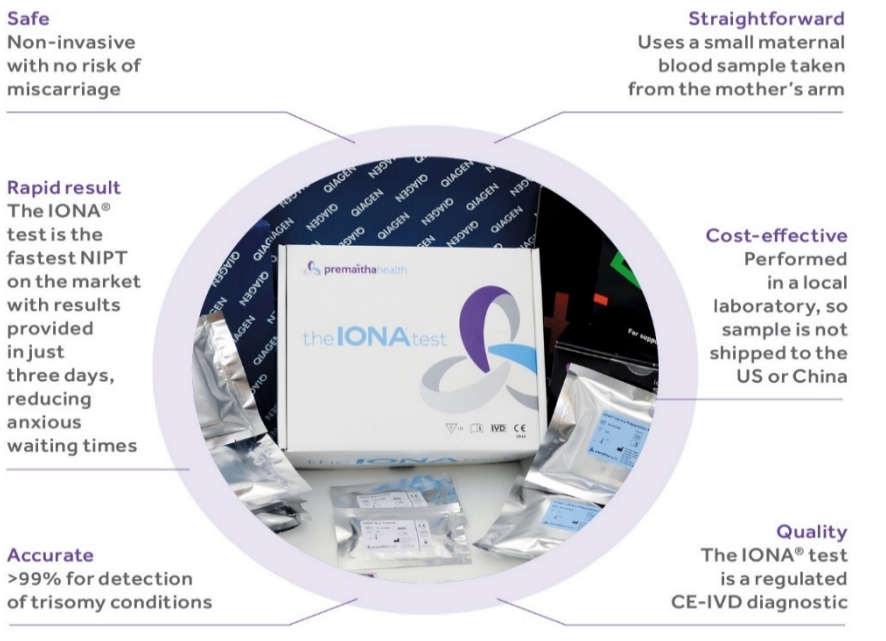
IONA® estimates the risk that a pregnant woman is carry a fetus with a genetic abnormality…

The IONA test is a non-invasive prenatal test (NIPT) for pregnant women which estimates the risk that their fetus might have trisomy of one or more of chromosomes 13 (Patau's syndrome), 18 (Edwards' syndrome) and/or 21 (Down's syndrome). The test is performed on a sample of maternal blood extracted after around 10 weeks of gestation and results are available in 3-5 days.

…IONA is extremely accurate with negligible false positives

The test estimates the risk of a fetus carrying an extra chromosome. Usually, cells contain 46 chromosomes – a child inherits 23 from each parent. In some circumstances, all or some of the cells in the fetus contain 47 chromosomes. Trisomies occur when three copies of a chromosome are present instead of the normal two, which occurs in Down's syndrome (Trisomy 21) and, more rarely, in Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13). Published independent trials indicate that the test is >99% accurate with negligible (or zero) false positives.

The IONA® test



Source: Premaitha Health

Commercialisation strategy

Premaitha has signed up eight countries to date but availability of IONA is more widespread

IONA is the first NIPT screening test that has received regulatory approval, via a CE Mark (February 2015). Subsequently, Premaitha has signed up with a number of clinical laboratories/distributors to make the test available in eight countries to date and there are many more immediate targets in Europe, Latin America, Middle East and Asia Pacific. In addition, Premaitha's clinical laboratory partner in Switzerland is drawing in and testing blood samples from other European countries, so the test is more widely available than would appear from the number of signed deals.

Availability of the IONA test

Announced deals		
UK (both NHS & private)	France	Greece
Switzerland	Poland	
Armenia	Moldova	Chile

Source: Premaitha Health

Commercial opportunity

About 140 million live birth per annum…

…60% of births are in countries offering prenatal screening…

…and ca.20% of births in developed countries are to women classified as high risk (aged >35 years)

Given that there are about 140 million births globally each year and that ca.60% of these are in countries that offer NIPT screening, the commercial opportunity is enormous. The statistics readily available in Europe and the US indicate that around 20% of these births are to 'high risk' women over the age of 35 years at parturition. This is the initial target market for the IONA test.

Live birth statistics — 2013

	Global	China	Europe	US	UK
Total births	136,800,000	18,500,000	5,075,380	3,932,181	778,800
Mother >35yrs	-	-	1,139,471	601,529	156,723

Source: WHO; Eurostat; ONS

Moreover, in the US, where reported sales from competitors indicate that the 'high risk' segment of the market is quite well penetrated, there is evidence that some pregnant women in the 'medium risk' segment (aged 25-35) are having the test performed for peace of mind. This segment is forecast to expand much more rapidly if test prices were to be reduced.

Commercial summary

Global market: $8.0bn…

US market $300m for high risk alone

European market $550m

Recommended availability of NIPT on NHS (UK) in high risk mothers

- **Global market**: $8.0bn based on 20% of live births to high risk women in countries where NIPT is available
- **US market**: $300m for the high risk category based on average price of $500 per test; some penetration of the average risk category which is expected to become routine over the next 25 months if prices are reduced to $250-500 per test. No products formally approved by the FDA
- **European market**: High risk market valued at $550m and currently a very low uptake of NIPT. Opportunity for IONA with CE Mark validation
- **UK market**: High risk market valued at $80m – Positive recommendation from National Screening Committee for NIPT testing on the NHS in high risk women announced 15th January 2016.

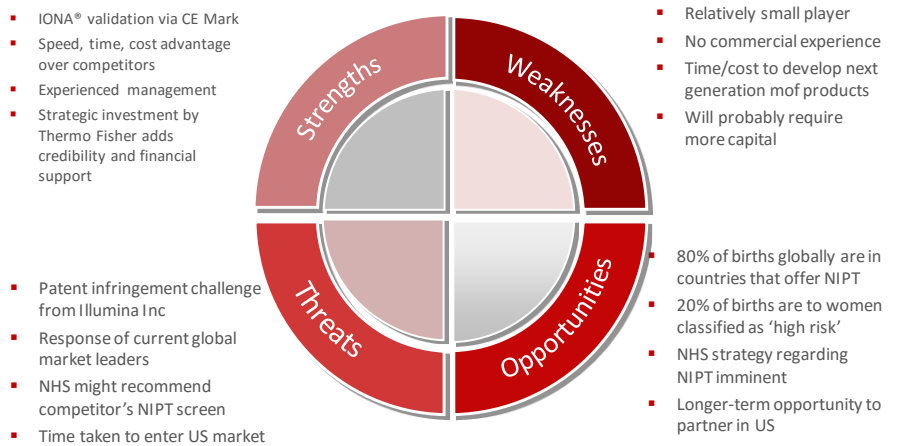
Apart from peace of mind, where the data is available, the accuracy of NIPT tests has been shown to cause a near 80% reduction in the use of invasive confirmatory amniocentesis and chorionic villus sampling, saving significant sums of money and reducing the risk of miscarriage.

Litigation update

Illumina has used the common tactic of tying up a potential threat through use of legal action

Shortly after Premaitha received CE Mark for IONA, the company was notified (March 2015) that one of its main competitors, Illumina Inc had filed patent infringement proceedings in the UK High Court. The patents asserted were EP0994963 (granted 14/05/2003) and EP1981995 (10/07/2013). In May 2015, Premaitha issued a vigorous defence of its position. In October 2015, Illumina added a third patent (EP2183693) to its case. In January 2016, Illumina broadened its IP claims by targeting Premaitha's Polish customer and also Roche's subsidiary Ariosa in the UK. In its Defence, Premaitha denies that it infringes the patents and Counterclaims for a declaration that the patents are invalid (Page 20).

SWOT analysis



Source: Hardman & Co Life Sciences Research

Investment by Thermos Fisher Scientific

In our opinion, TMO will have done considerable due diligence prior to making its £5m strategic investment in Premaitha

In December 2015, Thermo Fisher Scientific (TMO) made a £5m strategic investment into Premaitha (Page 35) which, apart from the cash resource, adds considerable credibility to the Premaitha story. Parts of the IONA test are rum on the TMO platform. Therefore, the aim of this agreement is to support the further development of the IONA test through product extensions and to improve the workflow efficiency of the screening process. Consequently, it reinforces the inherent link between Premaitha and TMO.

Investment conclusion

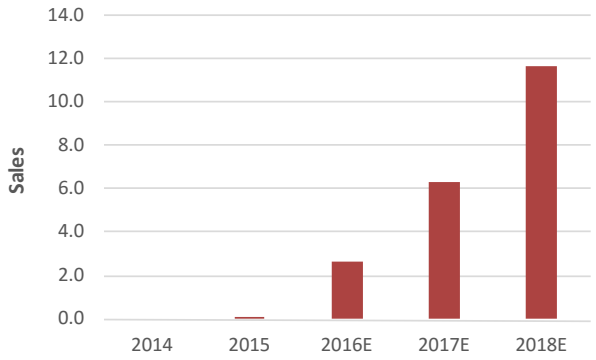
Premaitha will derive most of its sales from the less well developed European markets

Premaitha is trading on an enterprise value of £30m, compared to an R&D investment of ca.£5m to get the company where it is today. Its main quoted competitors with similar offerings are considerably more mature with more established sales, largely derived from the competitive US market. In contrast, Premaitha will derive the vast majority of its sales from the less developed markets of Europe and elsewhere in the medium term.

Acquirers have been willing to pay very high process for novel technologies and assets

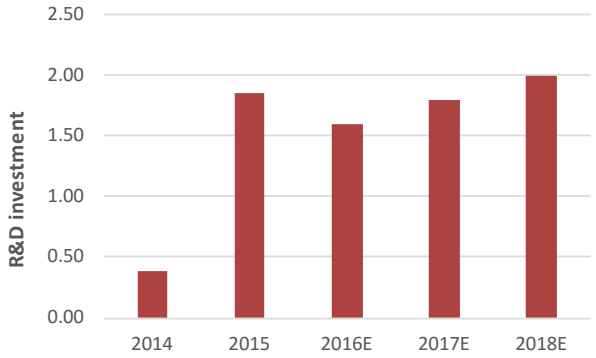
Alternatively, fair value can be determined by looking at the prices that acquirers were prepared to pay for novel technology and assets. Both Illumina and Roche, large players in diagnostics, have secured similar NIPT technology by buying smaller competitors – Verinata Health ($400m) and Ariosa ($625m) respectively – to access their products. However, it is again difficult to make a direct comparison to Premaitha because both these rivals were more advanced at the time of acquisition, and generating sales largely from the US market. But this does provide a guide about value when NIPT products have gained sales traction.

Sales development



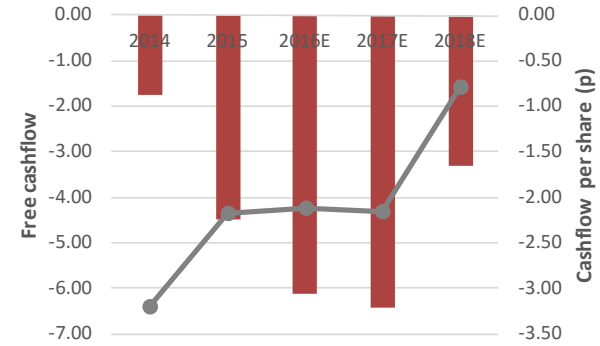
- Sales will mostly be derived from the supply of IONA kits or a a full service for blood samples sent to the company's laboratory for testing
- Some 'pass through' sales will be derived from strategic clients whose clinical labs are funded initially by Premaitha
- After signing contracts, there is an initial set-up/validation phase after which sales develop quite rapidly
- Monitoring 'sales/client' ratio will be a useful future guide (KPI) to sales growth

R&D investment



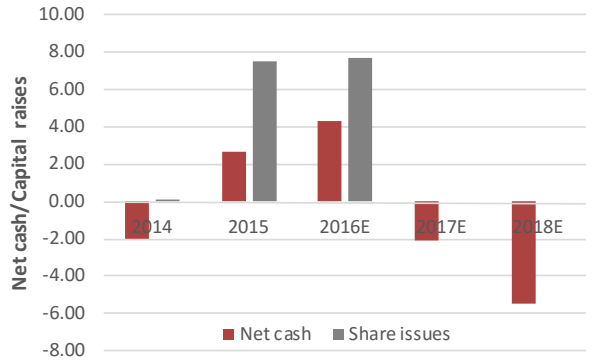
- An estimated £5m has been invested in R&D to get IONA to where it is today
- Further development to improve IONA functionality and increase Premaitha's offering will continue in future
- Management also intends to enhance the workflow efficiency of the test
- Liquid biopsies (early test for cancer) is an option in the future

Free cashflow



- Our forecasts for Premaitha are conservative, largely based on contracts/distribution agreements already announced
- Given that IONA has only been on the market for about six months, it is too early to predict uptake of the test
- Even on these cautious assumptions, Premaitha would approach cashflow breakeven towards the end of fiscal 2018
- Profitability and cashflows are extremely sensitive to small changes in sales forecasts

Net cash at 30th March



- At the end of September, Premaitha had cash of £6.6m
- This has been boosted by the £5.0m (first tranche: £3.0m) cash injection from TMO but, being in the form of a loan, it does not alter the net cash position
- Given sensitivity of forecasts to sales, announcements of new contracts would improve the year-end net cash postion
- In the event that Premaitha has to initially fund the establishment of strategic clinical labs, so a further capital injection might be required

Source: Company data; Hardman & Co Research

Prenatal screening

Prenatal screens are all part of the normal process of pregnancy…

…and take place at specific times during gestation

The pathway from conception through to newborn baby is excellently demonstrated in the timeline graphic shown on the following page. An expectant mother will be offered a number of screening tests during pregnancy to identify any potential health risks that could affect both mother and baby and allow choices to be made if any potential issues are identified.

Current abnormality screening procedures

- Weeks 8-12 — Blood for haemoglobin, blood group, rhesus, antibodies
- Weeks 8-12 — Also blood for syphilis, hepatitis, HIV and rubella
- Weeks 10-14 — Ultrasound + Blood for predicting Down's syndrome
- Weeks 15-20 — Blood for later Down's test
- Weeks 18-21 — Ultrasound anomaly scan

Combined test

The 'combined test' is a common early screen combining ultrasound with a biochemical blood test…

But does suffer from poor sensitivity and selectivity

The current test for Down's syndrome is called the 'combined test', where ultrasound is used to identify an increased level of fluid under the fetal skin at the back of the neck (nuchal transparency), coupled with a maternal blood test based on biochemical indicators. The advantage of this combined test is that it is performed during the same antenatal clinic and the results are available in about 40 minutes. The problem with this predictive test is that it has an accuracy of only 85% and high levels (3-5%) of false positives, which require invasive follow-up tests – chorionic villus sampling (CVS) or amniocentesis – both of which carry a risk of miscarriage and are very stressful for the pregnant woman. However, in the UK, until January 2016 only the 'combined test' was available free on the NHS and cost about £200/$300.

New DNA tests provides a far more accurate assessment…

…which should reduce the number of invasive confirmatory tests

The aim of the new DNA technology based tests, such as Premaitha's IONA test, is to provide a more accurate assessment of probability than combined test cases, thereby reducing the number of unnecessary and invasive confirmatory tests. The cost of the newer tests is about £300/$450.

Chorionic villus sampling

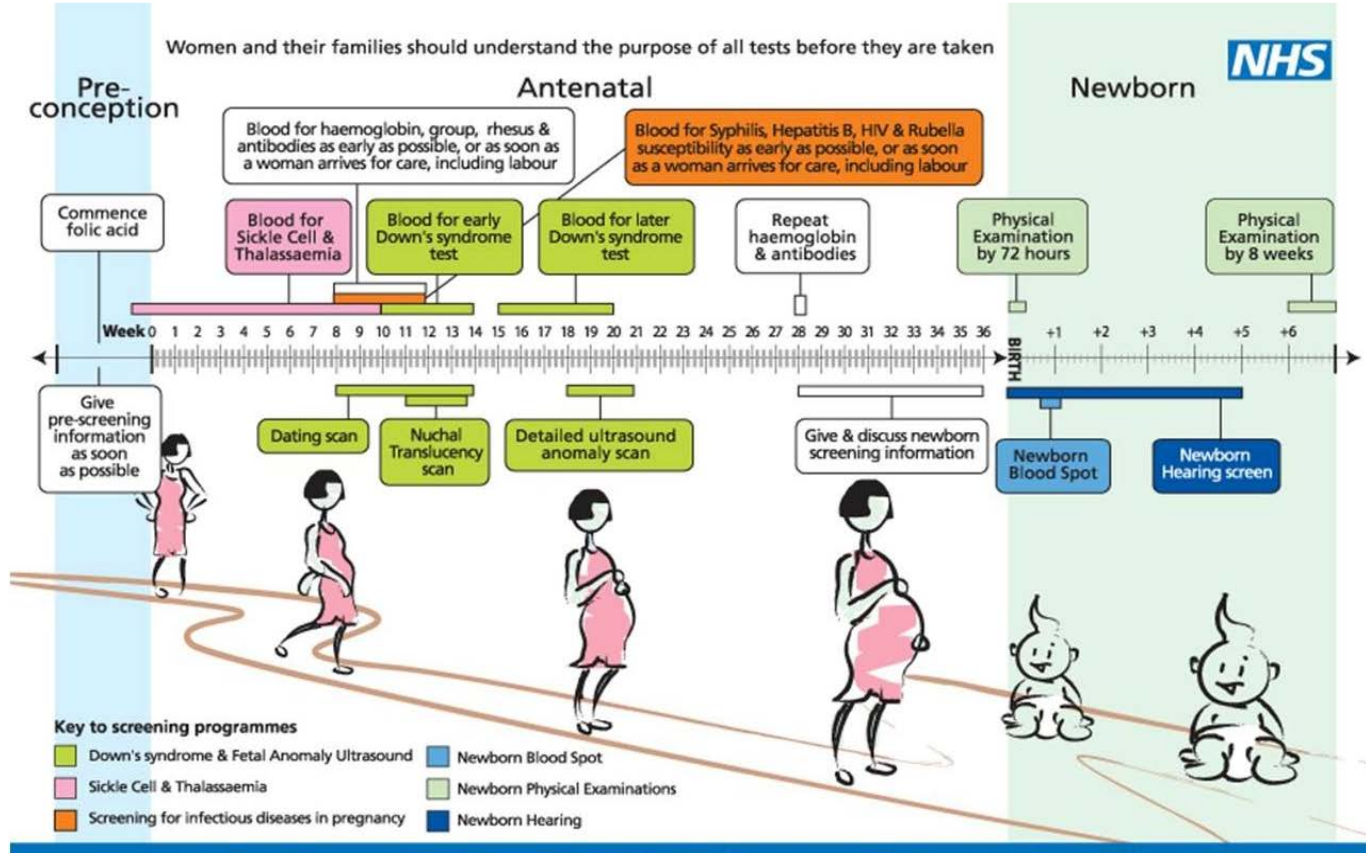
CVS is also a confirmatory test that is only offered during pregnancy to mothers where there is considered to be a high risk of a genetic disorder. It is carried out usually between 11-14 weeks of the pregnancy but can also be performed later if required. It costs £500-1,000 and is used as a confirmatory test for:

- Down's syndrome
- Sickle cell anaemia
- Cystic fibrosis or muscular dystrophy

During this procedure, a sample of cells is extracted from the placenta using one of two methods:

- Transabdominal CVS – via a needle
- Transcervical CVS – via forceps inserted through the cervix

Screening timeline – Optimum testing times



Source: NHS Choices

The procedure takes about 10 minutes and the results are normally available after 3 days. By its very nature, being an invasive procedure, there is also the associated small risk of miscarriage, estimated at about 1 in 100.

Amniocentesis

Amniocentesis is the best confirmatory test…

Amniocentesis is a diagnostic test which can assess whether a fetus could develop, or has already developed, an abnormality or serious health condition. It is carried out between 15-20 weeks of the pregnancy and is used as a confirmatory test for:

- Down's syndrome
- Spina bifida
- Sickle cell anaemia

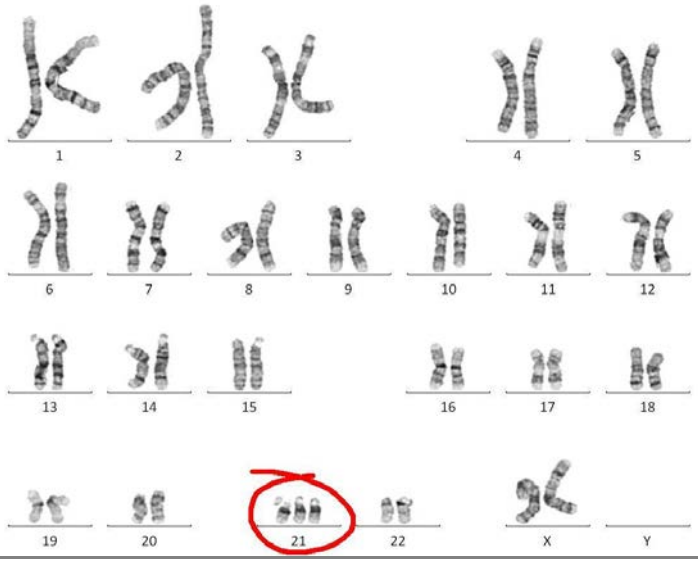
…but does carry a risk of miscarriage…

This procedure involves the insertion of a needle through the placenta to extract a sample of amniotic fluid which surrounds the fetus in the womb. This fluid contains cells shed from the fetus that can be tested for any defects.

…and is very stressful for the expectant mother

However, again, it is an invasive procedure and carries an associated small risk of miscarriage. Therefore, it is offered to pregnant women only where there is a high risk that the baby will develop a serious condition or abnormality. Results are normally available after 3 days (rapid test for chromosomal abnormalities) or 10 days (full karyotype of the 23 pairs of chromosomes). The estimated cost of an amniocentesis is £500-1,000.

Down's syndrome karyotype



Source: The NHS RAPID project

Non-invasive prenatal testing (NIPT)

Mother's blood contains a small quantity of fetal DNA…

…which can be tested to estimate the risk of a genetic abnormality

The goal of researchers for many years has been to develop a diagnostic test for Down's syndrome that does not involve an invasive procedure with the associated risk of miscarriage. This has resulted in the breakthrough of analysing the maternal blood which contains both the maternal and fetal cell-free DNA and simply involves a routine sample of blood at 10 weeks, with the key advantage of being 99% accurate. Such tests solve nearly all of the problems with existing tests and markedly reduce the number of invasive confirmatory tests required.

NIPT is available in about 60% of countries in which there are 80 million live births per annum. Of these, on average 20% are in mothers who are >35 years of age at parturition (high risk category). In the US, where NIPT is more readily available, data suggests that NIPT is being used more widely than the high risk category suggested in the regulatory guidelines.

On 15th January 2016 the UK National Screening Committee recommended that NIPT was made available routinely on the NHS to high risk pregnant women

Until January 2016, NIPT was available commercially in the UK through private clinics, but was not offered routinely by the NHS – although it was available at St George's Hospital Trust London. During 2015, an evaluation team, led by Professor Lyn Chitty (Great Ormond Street Hospital), reviewed how NIPT tests could be implemented by the NHS in a fair and affordable way. Her report was considered by the UK National Screening Committee which recommended on 15th January 2016 that NIPT should be made available routinely in the NHS to high risk pregnant women as part of the standard fetal prenatal screening programme for genetic anomalies. Data from the Office of National Statistics (ONS) indicate that more than 20% of live births in the UK classified as 'high risk' – mother aged >35 years at parturition.

In Europe, public bodies are assessing their proposals for reimbursement/coverage for NIPT tests. Early indications are that this will initially be for high-risk combined test results, but it is anticipated that Europe will follow the US example and move towards average-risk and then all-risk patients in due course. Switzerland is the first country to reach such a coverage decision but in 2016 decisions are expected in Denmark, France and other countries thereby moving NIPT testing from early private adopters and into mainstream publicly-funded healthcare.

The IONA®

What is the test?

IONA is performed on a sample of maternal blood taken at ca.10 weeks' gestation…and gives a result in 3-5 days

The IONA test is a non-invasive prenatal test (NIPT) for pregnant women which estimates the risk that their fetus might have trisomy of one or more of chromosomes 13 (Patau's syndrome), 18 (Edwards' syndrome) and/or 21 (Down's syndrome). The test is performed on a sample of maternal blood extracted after 10 weeks of gestation and results are available in 3-5 days.

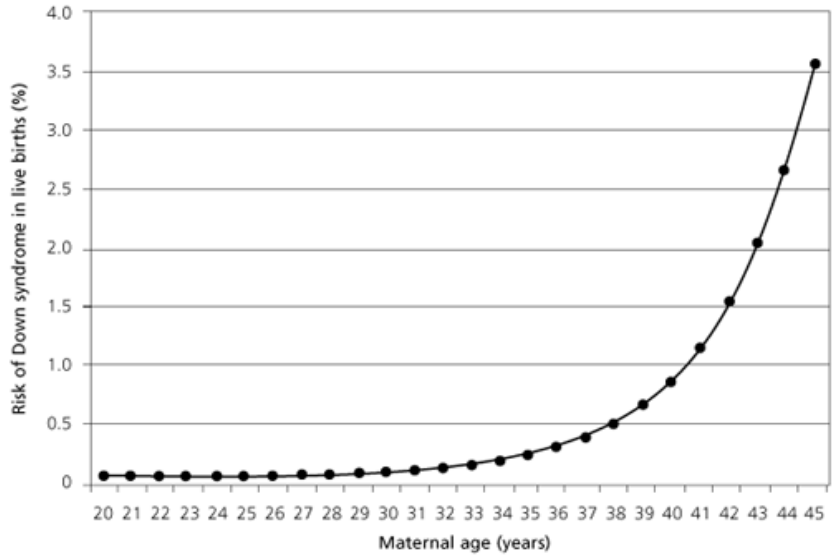
The test estimates the risk of a fetus carrying an extra chromosome. Usually, cells contain 46 chromosomes – a child inherits 23 from each parent. In some circumstances, all or some of the cells in the fetus contain 47 chromosomes. Trisomies occur when three copies of a chromosome are present instead of the normal two.

Down's syndrome – Trisomy 21

The risk of Down's increases significantly when the expectant mother is aged 35 or over

The most commonly recognised genetic cause of mental retardation and the risk of trisomy 21 is directly related to maternal age. Pregnant women who will be 35 years of age or older on the predicted birth date carry an increased risk of having a baby with Down's and are recommended to have a test. The risk of having a child with Down syndrome is 1/1,300 for a 25-year-old woman; at age 35, the risk increases to 1/300; by age 40, 1/100; and at age 45, the risk rises exponentially to 1/40. The chance of having a fetus with trisomy 21 is increased if there is previous history of an affected pregnancy. Also, there is a 1:2 chance if one of the parents has the condition. The estimated prevalence is 1 live births per 10,000 deliveries.

Age-related risk of Down's syndrome



Source: Cuckle et al[1]

The additional genetic material causes varying degrees of intellectual disability and physical and developmental characteristics – moon face, upward slanting eyes, unusually shaped or small ears, broad short hands, low height. Infants with Down's syndrome typically grow more slowly.

[1] Cuckle et al., *Br J Obstet Gynaecol*. 1987, 94:387–402.

Edwards' syndrome – Trisomy 18

Edwards' syndrome is a serious genetic condition caused by an additional copy of chromosome 18 – trisomy 18 – in all or some of the cells in the body. This causes disruption of normal fetal development often resulting in miscarriage or stillbirth. Having grown slowly in the womb, babies tend to have low birthweight along with a number of other medical problems. Of those that do survive to birth, ca.50% die within two weeks, only 20% survive three months and 8% one year. It affects about 1:6,000 live births.

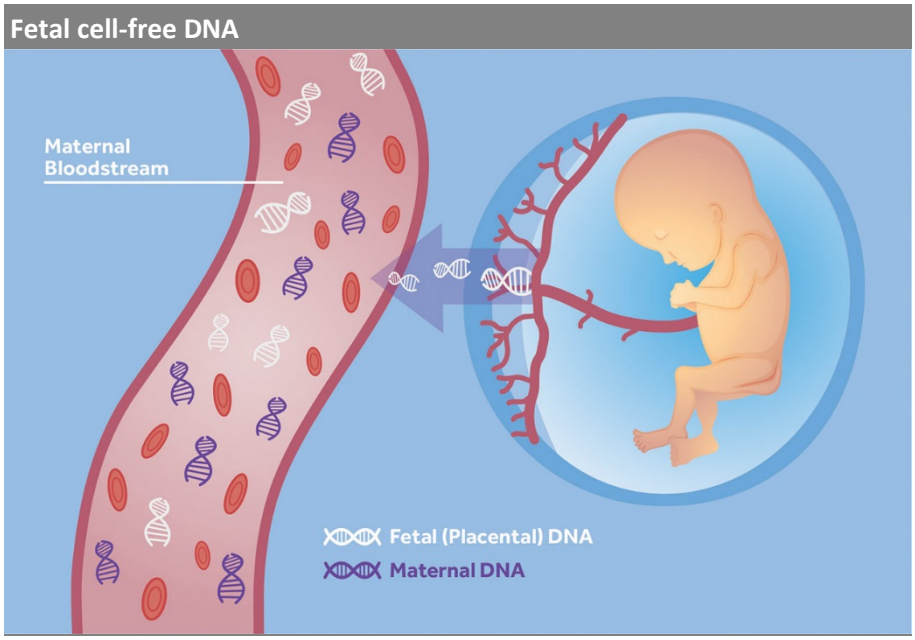
Patau's syndrome – Trisomy 13

Patau's syndrome is also a serious genetic condition caused by an additional copy of chromosome 13 – trisomy 13 – in all or some of the cell in the body. It is the least common and most severe of the autosomal trisomies, with a median survival of 3 days. It is generally recognised at birth by the presence of structural defects and poor neurological performance. It affects about 1:20,000 live births.

What is the technology?

NIPT are based around the fact that cell-free DNA from the fetus leaks across the placenta into the mother's bloodstream

During pregnancy, the feto-placental unit leaks cell-free DNA into the maternal bloodstream. Consequently, maternal blood contains a circulating mixture of maternal and fetal cell-free DNA. From a blood sample taken after 10 weeks of pregnancy, the IONA® test can identify small differences in the total number of cell-free fragments of DNA from chromosomes 13, 18 and 21 compared to fragments from other autosomes in the maternal plasma when fetal trisomy 13, 18 or 21 is present. The test uses Next Generation DNA Sequencing (NGS) technologies to count the number of chromosome fragments, which are analysed to provide an assessment of risk of an affected pregnancy.



Source: Premaitha Health

Who can have the test?

IONA is suitable for women at least 10 weeks into their pregnancy

IONA is suitable for all pregnant women carrying a single fetus, or twins, that was conceived through spontaneous conception, surrogates, or in-vitro fertilisation (IVF). Women need to be at least 10 weeks pregnant and the test requires a 10ml maternal blood sample.

What is the procedure?

IONA requires a maternal blood sample of 10ml…

From taking the maternal blood sample to receiving the test result involves a number of processes and takes about 3-5 days, dependent on whether the sample is analysed locally or sent to a central laboratory.

…which passes through a five stage workflow when it reaches the clinical test laboratory…

Maternal whole blood samples, taken after 10 weeks of gestation, are first separated by centrifugation to separate red blood cells from plasma containing the maternal and fetal cell-free DNA. The isolated DNA is then amplified in preparation for sequencing to allow the creation of millions of copies of the DNA fragments to generate a signal that is strong enough for detection of each cloned fragment. During analysis, the number of fragments derived from each chromosome is counted in order to predict whether the pregnancy is likely to be affected or unaffected.

…and results will be available after 3-5 days

A high risk outcome would then be verified by traditional invasive procedures, such as amniocentesis.

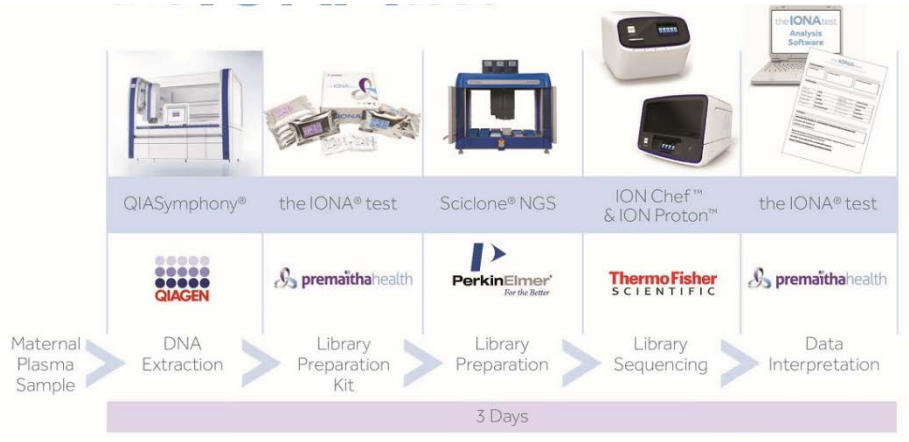
IONA test – workflow

Process	Activity
DNA extraction	Isolation of maternal and fetal cell-free DNA from plasma sample
DNA library preparation	Preparation of isolated DNA for sequencing and barcodes added to allow multiplex testing and subsequent decoding
Emulsion PCR	Creation of large numbers of cloned copies of each DNA fragment for sequencing reaction
DNA sequencing	Identification of the DNA sequence of each of the cloned fragments
Analysis	Counts the number of fragments derived from each chromosome and calculates whether the pregnancy is affected or unaffected

Source: Premaitha Health

The IONA test is performed on equipment that is standardised and validated for the required procedure. Premaitha co-ordinates with instrumentation partners and configures the system with server and software. If a new laboratory were to set up from scratch, the overall cost of the equipment and software to perform the IONA test would be in the region of $500k/£350k.

Test equipment & workflow



Source: Premaitha Health

How are results analysed?

Premaitha has developed and validated its own software analysis as part of the test workflow. This dedicated bioinformatics analysis employs highly efficient, multi-core algorithms.

- Automatically processes sequenced DNA fragments and clinical data
- Fast, user-friendly data entry and operation, and seamless connection to other components of the IONA workflow
- Test results exportable in common formats to support local off-line further analysis and test performance monitoring
- Interprets data to produce a customised report – available in local language
- Scalable turnkey solution of workstation and software, which is pre-configured and pre-installed
- Developed, verified and validated in compliance with IEC 62304 (Class C) and IEC 62366 medical device development standards

How are results reported?

The IONA test provides a clear report that is easy to interpret for the likelihood of the risk for each trisomy. A high risk outcome should always be confirmed with a follow-up invasive procedure.

- **Low risk**: Unlikely the pregnancy is affected by trisomy 21, 18, 13
- **High risk**: The pregnancy has increased risk for trisomy 21, 18, 13 and requires follow-up with amniocentesis
- **No result**: Valid result unable to be obtained, for example due to there being insufficient placental DNA in the sample to obtain a statistically reliable result. Re-test required with a new maternal blood sample

Clinical data

IONA is claimed to have >99% sensitivity …

The IONA test performs extremely well with official figures stating a sensitivity (detection rate) of >99% and a false positive of <1% in clinical studies when compared directly to results from amniocentesis samples.

…and <1% false positives

Supported claims[2]			
IONA test	**Syndrome**	**Detection rate (sensitivity)**	**False Positive Rate (FPR)**
Trisomy 21	Down's	>99%	<1%
Trisomy 18	Edwards'	>99%	<1%
Trisomy 13	Patau's	>99%	<1%

Source: Premaitha Health website

…but a recent independent study in 437 high risk women obtained 100% detection rate and 0% false positives

More recently, an independent study[3] was published from a double-blind UK multi-centre study that screened maternal blood samples from 437 high risk pregnant women for the three chromosomal abnormalities. Results showed a detection rate of 100% and a 0% false positive rate for the three tested conditions.

[2] http://www.premaithahealth.com/healthcare-professionals

[3] Papageorghiou et al., Journal of Ultrasound, Obstetrics in Gynecology. 2015 doi: 10.1002/uog.15791

Advantages of the IONA® test

The IONA test has a number of advantages, but key is the fact that a simple blood sample that can be taken during a normal antenatal clinic appointment will provide a highly accurate result in 3-5 working days.

Advantages of IONA

Advantage	Comment
Simple	Uses maternal blood which can be taken during normal antenatal clinic appointment
Safe	Non-invasive – no risk of miscarriage
Fast	Results available in 3-5 working days
Accuracy	>99% predictor of high risk pregnancy; <1% false positives
Quality	Regulated test with CE mark
Local	Performed in local clinical testing laboratory

Source: Premaitha Health; Hardman & Co Life Sciences Research

From a clinical perspective, IONA offers >99% accuracy compared to the current combined test – ultrasound + blood test, which has ~85% accuracy. Therefore, fewer pregnant women will require invasive follow-up procedures, which are stressful and carry a small, but increased risk of miscarriage.

Competitive landscape

Illumina and Roche are the main competitors

The landscape for NIPT tests is becoming increasingly competitive. Our research indicates that there are five main competitors to IONA – although there are many more brand names quoted on the web, many appear to be using the Verifi (Illumina) platform, which we consider to be the main competitor. MateriniT21 (Sequenom) has first mover advantage, but is in a patent pool arrangement with Illumina and predominantly available in the US market only.

Harmony (Ariosa/Roche) uses an alternative microarray process that operates on the Affymetrix technology platform. It should be noted that Thermo Fisher Scientific (TMO) agreed to acquire Affymetrix (AFFY) for $1.3bn on 11th January 2016.

Emerging battleground

Platform Technology	Testing Technology
Illumina	Illumina (+Sequenom + branded derivatives)
Thermo Fisher Scientific	Premaitha
	Ariosa/Roche

Source: Corporate websites; Hardman & Co Life Sciences Research

Product differentiation

All the products have similar outcomes…

As mentioned above, although most of the products are claiming similar outcomes, management believes that there are a number of differences in the processes used by Premaitha and that of the main rival, Illumina, with its Verifi test. At the outset, Premaitha undertook market research with clinical labs to understand key requirements for a prenatal screening test – automation and traceability – and the whole project has been driven to deliver these features.

…but there are differences in the processes and workflow…

…and some companies are offering extra features, at extra cost

The following table shows the test accuracy claimed in the product literature and on company websites, which are all very similar. Some companies are offering other features, for example, the sex chromosome and/or deletions for extremely rare conditions, mostly with no clear clinical pathway after diagnosis. Some of the turnaround times to results are long, primarily because the blood samples are being sent to the US for analysis. Prices are rarely quoted.

Sensitivity of competitive tests

Test	Harmony	IONA	MaterniT 21*	NIFTY	Panorama	Verifi
Manufacturer	Ariosa/Roche	Premaitha Health	Sequenom	BGI Diagnostics	Natera	Illumina
Platform	Affymetrix	Thermo Fisher	Illumina		Illumina	Illumina
Down's	>99%	>99%	99.1%	99.2%	>99%	99.1%
Edwards'	>99%	>99%	99.9%	98.2%	96.4%	98.3%
Patau's	>99%	>99%	91.7%	100%	>99%	98.2%
Others deletions	✓		✓		✓	✓
Time for result	7 days	3-5 days	5 days	10 days	9-12 days	7-10 days
Cost	$400-500	$150**/$450***	$800-900	$500	£500	$500**** – $800

**Available predominantly in the US market*
***Kit supply only*
****Full service + report*
*****via Birmingham Women's NHS Trust*
Source: Corporate websites; Hardman & Co Life Sciences Research

The workflow system described earlier is the culmination of working to satisfy the customer base:

- small lean systems with software to provide sample traceability
- reagents
- barcoded throughout
- CE Marked – both product and software

IONA treats the DNA fragment in a different way to Verifi

Key, however, is that IONA and Verifi treat the DNA fragments in different ways, the latter resulting in greater sampling time and more waste in order to achieve the same goal. The following table summarises some of the differentiating features between IONA and Verifi.

Differentiating IONA

IONA	Verifi
Available as a kit	Technology transfer
CE Mark (both products and software)	No CE Mark (possible on software, but not on reagents)
Class II device (High hurdle)	-
Fast turnaround (2.5 days + report)	7-10 days
NIPT reagents	Uses other suppliers' reagents
£350k to set up lab for 10-12,000 tests	Estimated at £1m

Source: Premaitha Health; Hardman & Co Life Sciences Research

In the competitive landscape table above, one important aspect that is not mentioned by companies involves the cost of the instrumentation required to run the test and the degree of complexity involved in running the test. As labs get more experience with these new tests, we expect to see an increasing level of differentiation which is not apparent from the sensitivity and false positive comparisons.

CE Mark on the 'whole test' gives comfort that the test has been fully validated

At present, one of the most attractive features of IONA compared to the competing products is that it has received full external quality accreditation and CE Mark. This give purchasers, whether they are clinical service labs (eg St George's NHS Trust) or kit purchasers, comfort that the product has been fully validated.

Comparison of tests		
Brand	**Supplier**	**Approach**
Harmony	Ariosa/Roche	Digital analysis of selected regions in an attempt to reduce time to result and cost by limiting sequencing to chromosomes of interest
IONA	Premaitha	Massively parallel sequencing (MPS) of whole DNA using ionosphere to amplify >100k times
MaterniT21	Sequenom	Uses MPS (shotgun approach) to examine more genetic material
Panorama	Natera	Single nucleotide polymorphism (SNP) technology which isolates and eliminates the maternal genotype thereby theoretically making the test on fetal DNA more accurate
Verifi	Illumina	Uses MPS (shotgun) of 36/72 sequences and uses fixed primers and light fluorescence for only four base pairs making the test more time consuming and expensive to run

Source: Corporate websites; Hardman & Co Life Sciences Research

Market opportunity

Global market opportunity

About 140 million live births per annum globally

There is an overwhelming quantity of statistics available on birth rates around the world, which, ultimately, equates to the target market. Given that the World Health Organisation states that there were 136.8 million live births globally in 2013, the market opportunity is enormous. However, we believe that it is more sensible to focus on a potential market that is more realistically achievable.

- Prenatal care involving at least four visits is offered in 64% of countries
- Only 58% (80 million) of live births were in countries that offer NIPT

Live birth statistics — 2013

	Global	China	Europe	US	UK*
Total births	136,800,000	18,500,000	5,075,380	3,932,181	778,800
Mother >35yrs	-	-	1,139,471	601,529	156,723

**included in Europe*
Source: WHO; Eurostat; ONS

In the developed world around 20% of live births are to 'high risk' women aged 35 years and above…

Using the statistic that about 20% of live births in countries offering prenatal care are in high risk women over 35 years of age, the potential opportunity in countries where NIPT is available is 16m tests per annum. At an average price of $500, this gives a global market opportunity of $8.0bn. In 2014, there were an estimated 1m NIPT tests performed, suggesting that the market has only been penetrated ca.6%.

…equating to 1.74m live births in the US and Europe

Focusing in on just the US and Europe, in 2013 there were just over 9.0m live births and 1.74m of these were cases where the maternal mother was in the 'high risk' category of >35years of age at parturition. For companies working in this space, trying to replace the relatively inaccurate 'combined test' with NIPT would be a natural first step. On the basis that an NIPT test (service + report) costs on average $500/£320, the high-risk addressable market in just the US and Europe equates to $870m.

United States

There are routinely about 4m live births in the US each year and about 0.6m of these are in high-risk women over the age of 35, where the use of NIPT is recommended in the regulatory guidelines, suggesting an annual market of $300m.

Penetrating the market – the US example

NIPT has penetrated the US market very successfully…

NIPTs were first launched in the US in late 2011 by Sequenom and in early 2012 by Illumina and Ariosa (Roche), all as Laboratory Developed Tests (LDT). In order to get some traction, these companies used key opinion leaders to provide clinical data and obtain product endorsement as a standard-of-care. At this juncture, there was no reimbursement, so the tests were often offered free of charge or as a loss leader, but this did generate some early traction.

In 2013, with greater experience and good clinical data, NIPT was endorsed by KOLs as a standard-of-care in high risk pregnant women. Some private insurers agreed to reimburse for the test in high risk cases. In 2013, Panorama (Natera) was launched as an LDT on to the US market, becoming the fourth entrant.

In 2014 and 2015, companies have been attempting to get NIPT more readily available to all pregnant mothers and are moving down into the medium and low risk categories, even though the regulatory guidance is for use in high risk expectant females only. The volume of tests rose significantly in 2014, but this coincided with about 17-20% reduction in average selling price (eg MaterniT21 average revenue per test was $1,170 in 2013 and $1,000 in 2014), as insurers reduced reimbursement levels and more NIPT providers entered the market.

…with just over 0.5m tests performed in 2014…

In the US, even in the absence of data from Illumina and sketchy data from Ariosa following its acquisition by Roche, we can identify the use of just under 0.5m tests in 2014, up from 0.3m in 2013. If tests are only being used in line with regulatory guidance, this would represent over 80% of the target market. This suggests that NIPT is being used much more widely than the recommended guidelines, even though it would not be reimbursed (primarily self pay).

US NIPT tests

2014	MaterniT21	Panorama	Harmony	Total
No. tests	162,600	185,000	150,000	497,600
Average price	$1,000	$680	n/a	est $700

Company reports; Hardman & Co Life Sciences Research

…which has resulted in a marked reduction in unnecessary confirmatory invasive tests

Importantly, however, analysis by Prof Diana Bianchi (Tufts University School of Medicine; Dondorp *et* al reference) suggests that there is a big overall cost benefit of NIPT. Given the accuracy of NIPT and that 97% of them are negative, this, coupled with the negligible false positive rate, has meant a 79% reduction in amniocentesis and a 69% reduction in chorionic villus procedures, which are very expensive. Apart from the cost benefit, these figures also do not take into account the stress and anxiety that these procedures cause.

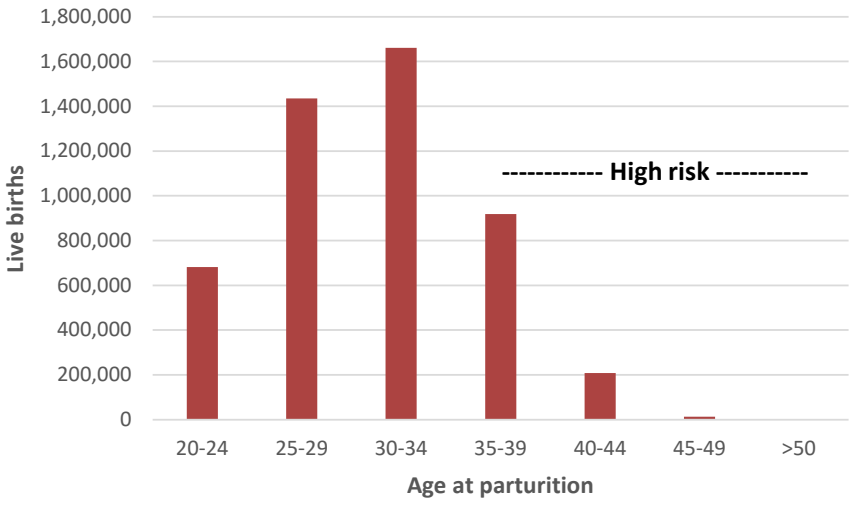
Europe

In contract, the European market is potentially twice as big…

…and poorly penetrated

In Europe (28 countries), there were 5.08m live births in 2013. Although 3.6m prenatal tests were performed, only about 50,000 used NIPT, compared to a target high risk population of 1.1m, a penetration of about 1.4%. At an average price of $500, the European market opportunity available to a product with CE Mark is estimated to be $550m.

Live births by age group in Europe – 2013



Source: Eurostat

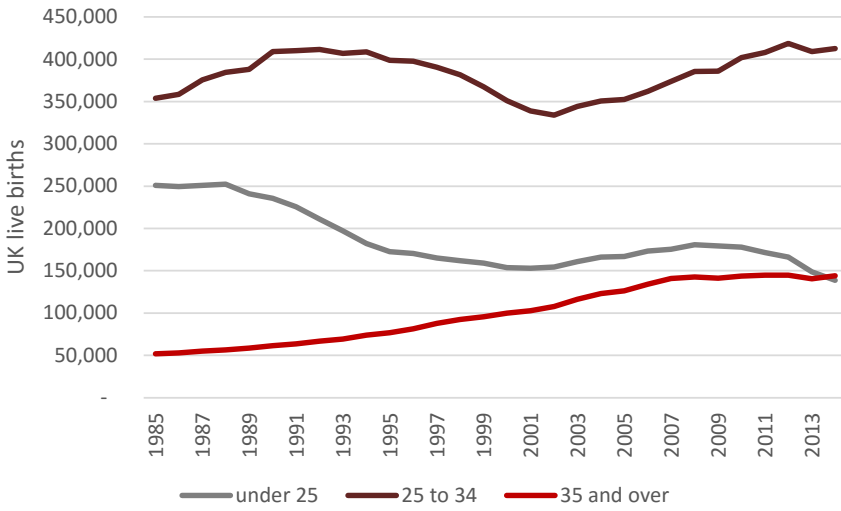
UK

Data from the Office for National Statistics (ONS) indicate that there were ca.157k births by high risk women over the age of 35 in 2014. However, until this year, although all expectant mothers have access to prenatal care through the NHS, NIPT was not part of the offering, with NIPT only available privately or through St George's University Hospitals Trust on the NHS.

January 2016…Major prenatal testing milestone in the UK

However, the UK National Screening Committee (NSC) commissioned a report by Dr Lyn Chitty from Great Ormond Street Hospital to evaluate how NIPT could be successfully implemented routinely within the NHS system without creating a huge burden of extra costs. Key to the evaluation and the argument for greater adoption of NIPT would be the suggestion by Bianchi et al that there would follow a marked reduction in the need for confirmatory invasive procedures. Having reviewed the report for over three months, on 15th January 2016, the NSC recommended that NIPT was made available to all high risk pregnant women where the risk of a Down's chromosomal abnormality was around 1:150. This represents a major milestone regarding prenatal testing in the UK and the decision is likely to be viewed and replicated in a number of countries globally.

Birth trend in England & Wales – 2014



Source: ONS

Summary

- **Global market**: $8.0bn based on 20% of live births to high risk women in countries where NIPT is available
- **US market**: $300m for the high risk category based on average price of $500 per test; some penetration of the average risk category which is expected to become routine over the next 25 months if prices are reduced to $250-500 per test. No products formally approved by FDA
- **European market**: High risk market valued at $550m and currently a very low uptake of NIPT. Opportunity for IONA as the only product with CE Mark
- **UK market**: High risk market valued at $80m – Market opportunity boosted by positive recommendation to make NIPT available free on the NHS by the UK National Screening Committee

Intellectual property

Premaitha is focused on protecting its intellectual property (IP) on a global basis wherever possible and, at the same time, constantly reviewing its Freedom-to-Operate (FTO) by avoiding the infringement of IP owned by third parties. For the protection of its own products, Premaitha has secured a number of patents, shown in the table at the bottom of the page.

Key application – WO/2014/033455

The most important of its patent applications is to the World Intellectual Property Organisation (WIPO) under the reference WO/2014/033455 which was made on 29th August 2013. The invention relates to a method of detecting chromosomal abnormalities and, in particular, to the diagnosis of fetal chromosomal abnormalities such as trisomy 21 (Down's syndrome) which comprises sequence analysis of cell-free DNA molecules in plasma samples obtained from maternal blood during gestation of the fetus.

The patent application describes the use of sequencing technology that might be prone to characteristic errors whilst offering the benefits of speed and cost ('economy grade' sequencing technology delivered by the 'Ion Torrent' platform). When this grade of sequencing is combined with Premaitha's proprietary and validated analysis software, it can exploit the characteristic inaccuracies to extrapolate the fetal chromosomal abnormalities.

Freedom-to-operate

In addition to protecting its own property, Premaitha has commissioned confidential and legally privileged FTO reports over recent years to ensure that the IONA test does not infringe the intellectual property of other companies working in a similar space. Apart from their importance in the normal course of business of the company, these reports formed an important part of the due diligence process required when Premaitha sought its listing on the London Stock Exchange in 2014. Therefore, it was a surprise when Premaitha announced to the market in March 2015 that Illumina Inc and its wholly owned subsidiary, Verinata Health Inc, filed a patent suit in the UK against Premaitha asserting that its assigned patents EP0994963 (Non-invasive prenatal diagnosis; ISIS Innovation Ltd) and EP1981995 (Non-invasive digital fetal genetic screening by digital analysis; Stanford University) had been infringed.

In October 2015, Premaitha announced that Illumina had extended the infringement claim in the UK to include a third patent, EP2183693 (Diagnosing fetal chromosomal aneuploidy using genomic sequencing; Chinese University of Hong Kong). Suffice to say, Premaitha is vigorously defending these claims.

Intellectual property

Patent no.	Country	Description	Filed	Status	Granted	Expiry	Applicant
US11/036833	US	Nucleic acid detection	14 Jan 2005	Granted	7 Aug 2007	27 Jan 2026	Zoragen Biotech
US11/909557	US	Nucleic acid detection	23 Mar 2006	Granted	4 Feb 2014	23 Mch 2026	Zoragen Biotech
US13/996303	US	Nanopore prenatal diagnosis	20 Dec 2011				Loxbridge Research
EP2655655 EP11804760.4	EU	Nanopore prenatal diagnosis	20 Dec 2011	Intention to grant			Premaitha Health
WO/2014/033455	PCT	Prenatal scoring for detection of chromosomal abnormalities	29 Aug 2013				Zoragen Biotech

Source: Company reports; Hardman & Co Life Sciences Research

Patent challenges extended

In January 2016, Illumina extended its IP claims by filing two patent infringement lawsuits in Europe. First, it filed against Premaitha's customer in Poland along the same lines that it has used against Premaitha in the UK. Secondly, it took a similar action against Roche, its wholly owned subsidiary Ariosa, and its main customer in the UK – The Doctors Laboratory.

Conclusion

Although we are not experts and have to rely on publicly available information, it appears that Premaitha has a very strong case in its defence against Illumina's patent infringement claims. Therefore, the question arises as to "what does Illumina hope to achieve?" We have seen many times before, situations where big global companies are worried that they might be behind the curve on technology and will do anything to protect their considerable investment and business. Such companies know that, with strong cashflow and deep pockets, they have a huge advantage in tying up small less well capitalised companies in litigation for many years and in our opinion, this is Illumina's strategy with Premaitha. Furthermore, this strategy is not without precedent, Illumina having travelled down this pathway three times before with NIPT companies:

- **Verinata Health**: Illumina ended up buying the company
- **Sequenom**: Illumina paid $50m and agreed to pool its patents with Sequenom and work together to expand the market (full details in Sequenom 2014 10-K)
- **Ariosa** (now Roche): Illumina's challenge was thrown out in the courts, but the claims were different in this case

In Premaitha's 2015 accounts, a provision of £0.5m was made to fight Illumina and defend its position in the courts. However, this was based on the initial challenge claiming infringement of two patents. Subsequently, Illumina added the third patent, and within its announcement of the 2016 interim results, management increased the litigation provision to £1.9m.

First action listed for October 2016

Unfortunately, by its very nature, litigation can be a relatively slow process. A trial in the first action is listed for early October 2016, the earliest that a trial on the second action could take place appears to be early 2017. Furthermore, it is likely that there will be an appeal by whichever party is unsuccessful following the judgment at first instance. Meanwhile, Premaitha simply has to get on with the task of establishing IONA as one of the most efficient to perform prenatal tests in the market.

Financials & Investment case

Given that Premaitha was established only in 2013 and reversed into ViaLogy in 2014, there is minimal historical financial information. All the financials regarding ViaLogy are completely irrelevant as current operations have nothing to do with that company's businesses.

Profit & Loss

Sales

As IONA becomes better established, Premaitha will derive three sales streams

As the IONA test becomes better established as a prenatal screen, Premaitha will essentially have three sales streams:

- **IONA test kit** – sales of the kit to clinical testing labs and overseas distributors for an estimated £100-150 per kit
- **Full service sales** – where blood samples are sent to Premaitha's labs to be analysed for an estimated £200-250 per test
- **Pass through sales** – Premaitha pays for the equipment required to set up a clinical testing facility and recovers this cost (eg St George's Hospital, London). The margin on this will essentially be zero, with Premaitha making money out of the subsequent supply of test kits

Although Premaitha will runs its own laboratory service, it is anticipated that the majority of sales will come from the supply of kits to clinical labs and distributors

The majority of Premaitha sales will come from either the supply of kits (and reagents) to perform the IONA test, or providing a full test service to clients that send blood samples to the company's laboratory. In some circumstances, Premaitha will fund strategic clients by paying the cost of setting up their laboratories and recover this outlay through leases, reagent rental, or profit share. In the short-term, depending on how many clinical testing labs are established, the sales line could be quite lumpy.

The IONA kit comes as a fully bundled price for undertaking the test which includes some ancillary consumables – bespoke plastics and OEM reagents for running the QIAGEN and Thermo Fisher platforms – to perform the test. While it is feasible to have everything together in a single kit for local (UK and EU) markets, this does not necessarily work in overseas markets, therefore, a degree of unbundling may result for some territories.

Commercial agreements

Key commercial agreements to date

Date	Country	Partner	Agreement type	Comment
5 Feb 2015	CE Mark Europe			
16 Mch 2015	Switzerland	Genoma SA	Clinical testing lab	Under TRANQUILITY brand
23 Mch 2015	UK	St George's NHS Trust	NHS clinical testing lab*	First availability free on NHS
31 Mch 2015	Poland	Centrum Baden	Clinical testing lab	Private screening availability
2 Oct 2015	Greece	Antisel SA	Distributor	Supplies network of clinical labs
13 Oct 2015	UK	Wolfson Institute	Clinical testing lab*	Charitable (part NHS) screening service
2 Dec 2015	France	Adgenix	Exclusive distributor	
2 Dec 2015	France	LaboSud	Private testing lab	Minimum 3-year contract

**Initially samples sent to Premaitha for service testing*

Source: Company announcements; Hardman & Co Life Sciences Research

To date, Premaitha has signed eight supply, service and distribution agreements

Since receipt of CE Mark in February 2015, Premaitha has signed eight supply, service and distribution agreements, which we anticipate will rise to 10 by the end of the current financial year (March 2016). The six listed in the table above are the most significant in terms of market opportunity. As the sales model becomes better developed and more commercial agreements get signed, we expect to use sales per contract as a key performance indicator (KPI), which will provide an objective method of growth. Based on initial sales reported in the recent interim results, for 1H 2016, this ratio was £155k per active client.

Gross margin target is 50%

Gross margins

The stated target gross margin for IONA is 50%. However, in the short-term, while clinical labs and distribution networks are being established, this is likely to be nearer 40-45% and will build-up quickly with volume to the target level. In addition, for clarity, our models exclude 'pass through' sales in the calculation of gross and EBIT margins as these will artificially bias the forecasts and outcomes.

Ongoing SG&A growth of 8-10% is forecast

Marketing (SG&A)

Given that the group strategy is the rapid commercialisation of the IONA test, there has been an inevitable increase in marketing investment during 2016, to an estimated £4.4m. Although marketing investment will continue as the management expands the test availability into more territories, growth in spending is forecast to be at a much slower rate (8-10%) in future years.

No need for further major R&D investment

R&D

Most R&D required for the commercialisation of the IONA prenatal screen has been made already. Therefore, we do not anticipate any large increase in R&D in the medium term. Some investment is likely in order to improve the workflow efficiency. In addition, we would expect Premaitha to add further parameters to the current test, as evidenced by the recent addition of sex determination (optional where allowed by law), to make it more comparable to some of the competing tests.

Longer-term, further investment in R&D could result in liquid biopsies, whereby similar DNA analyses could reveal the early diagnosis of other conditions prior to the observation of symptoms, eg cancer.

Our conservative forecasts suggest that Premaitha will become EBITDA positive in fiscal 2018

Profitability

Our forecasts are based on an assumed 10 contracts in fiscal 2016, rising to 15 in 2017 and 20 in 2018. After signing contracts, we assume that there is a three month time lag – installation phase – before kit sales are made, typified by the St George's contract which was nearer six months. Following this, there will be a ramp-up phase before the clinical labs are running at their greatest efficiency – 800–1,000 tests per month. On this basis, our model suggests that Premaitha will become EBITDA positive in fiscal 2018.

Sales for 2016 likely to be nearer £2.5m than our earlier forecast of £2.0m

Changes to forecasts

Until publication of initial IONA sales in the 2016 interim results, forecasts were somewhat 'blind'. However, we were very encouraged by the first-half sales outcome, with a sales/active contract ratio of £150k. Extrapolating this forward, our kit/service sales forecast for 2016 has increased from £1.7m to £2.25m and for fiscal 2017, from £5.0m to £5.8m. These figures are likely to rise further as more contracts are signed. Such changes would increase the probability that Premaitha becomes EBITDA positive in Fiscal 2018.

Profit & Loss account					
Year end March (£m)	**2014**	**2015**	**2016E**	**2017E**	**2018E**
IONA kit sales	0.00	0.00	1.85	4.36	7.91
Service income	0.00	0.00	0.25	1.20	2.40
Pass-through sales	0.00	0.00	0.35	0.50	1.00
Other	0.00	0.00	0.05	0.15	0.30
Total sales	**0.00**	**0.00**	**2.50**	**6.21**	**11.61**
COGS	0.00	0.00	-1.21	-2.97	-5.31
% sales	nm	nm	56.0%	52.0%	50.0%
SG&A	-1.25	-2.62	-4.40	-4.84	-5.23
% sales	nm	nm	nm	nm	49.3%
R&D	-0.38	-1.85	-1.60	-1.80	-2.00
% sales	nm	nm	74.3%	31.5%	18.8%
EBITDA	**-1.44**	**-4.08**	**-4.22**	**-2.69**	**0.01**
Deprec & Amortis	-0.08	-0.26	-0.48	-0.71	-0.93
Other income	0.10	0.13	0.00	0.00	0.00
Underlying EBIT	**-1.53**	**-4.34**	**-4.70**	**-3.40**	**-0.92**
EBIT margin	nm	nm	nm	-54.7%	-7.9%
Share based costs	0.00	-0.35	-0.60	-0.60	-0.60
Statutory EBIT	-1.53	-7.54	-6.72	-4.00	-1.52
Net financials	0.00	0.09	0.05	-0.15	-0.26
Pre-tax profit	**-1.53**	**-7.45**	**-6.67**	**-4.15**	**-1.78**
Exceptional items	0.00	0.00	0.00	0.00	0.00
Reported pre-tax	-1.53	-7.45	-6.67	-4.15	-1.78
Taxation	-0.04	0.00	0.00	0.00	0.00
Tax rate	nm	nm	nm	nm	nm
Underlying net income	**-1.57**	**-7.43**	**-6.67**	**-4.15**	**-1.78**
Statutory net income	-1.57	-7.43	-6.67	-4.15	-1.78
Weighted average shrs (m)	37.95	151.89	217.42	228.16	228.16
Fully diluted shares (m)	37.95	182.38	277.91	288.65	288.65
Underlying Basic EPS (p)	**-4.13**	**-4.89**	**-3.07**	**-1.82**	**-0.78**
U/l Fully-diluted EPS (p)	-4.13	-4.07	-2.40	-1.44	-0.62
Statutory Basic EPS (p)	-4.13	-4.89	-3.07	-1.82	-0.78
Stat. Fully-diluted EPS (p)	-4.13	-4.07	-2.40	-1.44	-0.62
DPS (p)	0.00	0.00	0.00	0.00	0.00

Source: Hardman & Co Life Sciences Research

Balance sheet

- The net cash position is influenced by the long-term debt (£5m) drawdown from TMO, which we anticipate will be over the next three years
- Based on our assumptions, the company has sufficient cash until the end of fiscal 2017 for its working capital requirements
- The provision for litigation costs currently stands at £1.9m, of which about £0.12m has been spent already

Balance sheet

@ 31st March (£m)	2014	2015	2016E	2017E	2018E
Share capital	8.28	28.17	32.17	32.17	32.17
Reserves	-9.84	-24.28	-26.95	-31.10	-32.88
Minorities	0.00	0.00	0.00	0.00	0.00
Capitalised R&D	0.00	0.00	0.00	0.00	0.00
Provisions	0.00	0.12	1.67	0.67	0.00
Deferred tax	0.04	0.04	0.00	0.00	0.00
Long-term loans	1.50	0.00	3.00	4.50	5.00
Bank overdrafts	0.54	0.00	0.00	0.00	0.00
less: Cash & securities	0.05	2.71	7.25	2.31	-0.50
less: Marketable securities	0.00	0.00	0.00	0.00	0.00
less: Non-core investments	0.00	0.00	0.00	0.00	0.00
Invested capital	**0.47**	**1.35**	**2.65**	**3.94**	**4.80**
Fixed assets	0.44	1.35	2.36	3.16	3.72
Intangible assets	0.00	0.00	0.00	0.00	0.00
Tax asset	0.25	0.80	0.40	1.00	1.00
Capitalised R&D	0.00	0.00	0.00	0.00	0.00
Stocks	0.00	0.45	0.65	0.95	1.14
Debtors less creditors	-0.22	-1.25	-0.77	-1.17	-1.07
Invested capital	**0.47**	**1.35**	**2.65**	**3.94**	**4.80**
Net cash/(debt)	-1.99	2.71	4.25	-2.19	-5.50

Source: Hardman & Co Life Sciences Research

Cashflow

Year end March (£m)	2014	2015	2016E	2017E	2018E
Trading profit	-1.53	-4.34	-4.70	-3.40	-0.92
Depreciation	0.08	0.26	0.48	0.71	0.93
Amortisation	0.00	0.00	0.00	0.00	0.00
Stocks	0.00	-0.45	-0.20	-0.30	-0.19
Working capital	0.23	0.64	-0.80	-1.10	-1.32
Exceptionals/provisions	0.00	0.00	-0.40	-1.10	-0.50
Disposals	0.00	0.10	0.00	0.00	0.00
Other	0.00	0.14	0.00	0.00	0.00
Company op cashflow	**-1.22**	**-3.65**	**-5.62**	**-5.19**	**-2.00**
Net interest	0.00	0.09	0.05	-0.15	-0.26
Tax	0.00	0.25	0.90	0.40	0.45
Operational cashflow	-1.22	-3.30	-4.67	-4.94	-1.81
Capital Expenditure	-0.52	-1.17	-1.50	-1.50	-1.50
Sale of fixed assets	0.00	0.00	0.00	0.00	0.00
Free cashflow	**-1.74**	**-4.47**	**-6.17**	**-6.44**	**-3.31**
Dividends	0.00	0.00	0.00	0.00	0.00
Acquisitions	0.00	0.00	0.00	0.00	0.00
Disposals	0.00	1.23	0.00	0.00	0.00
Other investments	-0.28	0.00	0.00	0.00	0.00
Cashflow after investments	**-2.01**	**-3.24**	**-6.17**	**-6.44**	**-3.31**
Share repurchases	0.00	0.00	0.00	0.00	0.00
Share issues	0.00	7.48	7.72	0.00	0.00
Currency effect	0.00	0.00	0.00	0.00	0.00
Borrowings acquired	0.00	0.46	3.00	1.50	0.50
Change in net cash/(debt)	**-2.01**	**4.70**	**4.54**	**-4.94**	**-2.81**
Hardman FCF/S (p)	-3.20	-2.18	-2.15	-2.17	-0.79

Source: Hardman & Co Life Sciences Research

Cashflow

- Investment in the commercial strategy leaves monthly cash burn in the range of £600-700k per month
- The TMO investment (initially £3.0m) has boosted the company's cash position by £3m but, being in the form of a loan, has no effect on the net cash position
- Based on the expected increase in both the number of contracts and the sales/contract, our forecasts suggest that Premaitha will be cash generative in fiscal 2019

Valuation

Comparative valuation

Premaitha is trading on an enterprise value of £30m, compared to an R&D investment of ca.£5m to get the company where it is today. Whether this is a true reflection of valuation is difficult to say. First, its main quoted comparators are considerably more mature companies with much larger sales that are derived from the large, but competitive US market. In contrast, Premaitha will derive the vast majority of its sales from the less developed markets of Europe and other regions in the medium term. Secondly, Premaitha's competitors are operating in a market where products are less regulated (LDT vs CE Mark) and prices are under intense pressure, which has resulted in considerable share price underperformance.

Comparative valuation

	Natera	Sequenom	Premaitha
	NTRA	SQNM	NIPT
	$/$m	$/$m	£/£m
Share price	9.06	1.54	0.17
Shares (m)	50.0	118.6	228.2
Sales	185	130	2.6
Market cap	453	183	39
Net cash/(debt)	244	-84	7
EV	209	267	32
EV/sales	1.1	2.1	11.9

Prices at close of business on 22nd January 2016
Source: Hardman & Co Life Sciences Research

Take-out valuations

Another way of determining valuation looks at the prices that acquirers have been prepared to pay for the novel technology and assets. Both Illumina and Roche have secured the latest NIPT technology by buying smaller competitors to access their products. However, it is again difficult to make a direct comparison to Premaitha because both companies were more advanced and generating sales largely from the US market. But this does provide a guide about value when NIPT products have gained sales traction.

NIPT take-out valuations

Date	Acquirer	Target	Up-front	Deferred	Total	Comments
Feb 2014	Illumina	Verinata	$300m	$100m	$400m	$100m development costs over 10 years
Dec 2014	Roche	Ariosa	$400m	$225m	$625m	Sales $53m (2013); $45m invested

Source: Hardman & Co Life Sciences Research

Conclusion

In conclusion, Premaitha has made considerable progress in its early commercialisation of IONA. This looks set to accelerate as more commercial deals are signed to expand its availability into more territories. The USP is that, outside China, IONA is the only product to be validated with CE Mark, which provides added comfort to purchasers/licensees. We believe that its progress will be closely monitored, not only by competitors for commercial reasons, but also by its suppliers and those companies that are currently quite large players in the biochemical-based 'combined test' market but have no access to the next generation DNA sequencing NIPT products, such as Siemens, Perkin Elmer and Phillips.

Company matters

Registration

Incorporated in the UK with company registration number: 3971582

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Pencroft Way
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Registered Office
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Gloucestershire
GL50 3PR

+44 161 667 6865
www.premaitha.com

Board of Directors

The Board consists of four executive directors and four non-executive directors, including the Chairman. Their representation on the various committees is shown in the following table.

Board of Directors

Position	Name	Nominations	Remuneration	Audit
Chairman	David Evans	C	C	M
Chief Executive Officer	Dr Stephen Little			
Chief Financial Officer	Barry Hextall			
Chief Business Officer	Peter Collins			
Chief Medical Officer	Dr William Denman			
Non-executive director	Nicholas Mustoe (Senior independent)	M		M
Non-executive director	Adam Reynolds	M	M	C
Non-executive director	Dr Charles Roberts	M		

M = member; C = chair
Source: Company reports

David Evans – Non-executive Chairman

David is well known in the Life Sciences arena having a proven track record in acquiring, integrating and growing businesses in the diagnostic space and in value creation, exemplified by his role at BBI Holdings plc where he grew the company both organically and through acquisition, from a value of £4m to £84m by 2007, when it was sold to Inverness Medical Innovations Inc. He was chairman of DxS Limited ("DxS"), which was sold three months after his departure in 2009 for £82m. David was also chairman of Sirigen Group Limited, an early stage medical technology company that was sold in 2012 to the global medical technology company Becton, Dickinson. David was previously Chairman of Immunodiagnostics Systems Holdings plc, Epistem plc, EKF Diagnostics plc and Scancell Holdings plc. Apart from Premaitha, David is currently chairman of Omega Diagnostics Group plc, Collagen Solutions plc, Optibiotix plc and Venn Life Sciences Holdings plc.

Dr Stephen Little – Chief Executive Officer

Stephen is a successful serial biotechnology entrepreneur and previously work with the Chairman at DxS, a company specialising in the field of personalised medicine. This Manchester-based company was funded with £3.5m in 2001 and was sold to QIAGEN BV in 2009 for £82m. During that time DxS pioneered the use of molecular diagnostic tests such as KRAS and EGFR mutation analysis to predict the use of novel cancer therapies. The legacy of DxS is a major global *in vitro* diagnostic business within QIAGEN employing over 250 people which continues to develop and expand at its European headquarters in Manchester. Following this success, Stephen joined Premaitha and has assembled a talented and experienced team of individuals with the skills, knowledge and background needed to address both the technical and commercial challenges of bringing a prenatal screening product to market.

Barry Hextall – Chief Financial Officer

Barry was appointed as CFO on 4th June 2015. He is a Chartered Management Accountant with over 15 years' experience in senior financial roles at a number of companies, including AIM-listed entities. He has managed many international businesses through major changes and rapid growth, and has significant experience working in the fields of medical devices and diagnostics. His previous employers include JRI Orthopaedics Ltd, Immunodiagnostic Systems plc, C J Garland & Co Ltd, Ernst & Young LLP and Zeneca (formerly ICI) plc.

Peter Collins – Chief Business Officer

Peter is a seasoned executive in molecular diagnostics and provides a wealth of experience in strategic leadership, business development and commercialisation. Peter has joined Premaitha Health from a prestigious role as Vice President, Head of Diagnostics at GSK, where he led its Diagnostic Nucleus focused on supporting the diagnostic needs of GSK's Clinical Development Programs across all business units.

Peter was formerly Vice President of Pharma Business Development for QIAGEN driving the uptake of companion diagnostic programs in multiple partnerships across the pharma industry. Before this he was VP Business Development at DxS prior to its acquisition by QIAGEN in September 2009. Peter was also VP of Marketing and Sales for Vysis Europe (now Abbott Molecular Diagnostics), where he led the introduction PathVysion Her2 for selection of patients eligible for Herceptin in the EU.

Peter has strong entrepreneurial background and has held senior executive roles, including CEO, at a number of early stage diagnostics and life sciences companies including Quantase (Bio-Rad) where he worked in the field of prenatal screening. Further executive roles have been held at Gentronix, Biogenex and Pronostics. He began his commercial diagnostic career with Syva (Dade Behring/Bayer/Siemens) and BD's Immunocytometry division. Peter is a founder and held a board position for two years at EPEMED, a not for profit European organisation to bring together global forces in personalised medicine.

Dr William Denman – Chief Medical Officer

Dr Denman MB instructs at Massachusetts General Hospital, specialising in paediatric anaesthesia and medical device development. He is Principal of Denman Associates and was former CMO of Loxbridge Research LLP. Pepper has significant experience in the clinical aspects of device and diagnostic development. His previous role was as CMO with GE Healthcare with primary responsibility for all matters of patient safety in this multi-billion dollar business. Prior to this he was at Covidien where he was responsible for strategic direction of medical affairs, clinical affairs and

healthcare economics and outcomes across Covidien's entire medical device sector. Pepper studied medicine at the University of Aberdeen.

Nicholas Mustoe – Senior independent Non-Executive Director

Nick started his career in 1981 working in London advertising agency Foote Cone and Belding followed by nine years at Lowe Howard Spink working with a number of blue-chip companies. In 1993, he started and ran his own agency, Mustoes Merriman Levy (Mustoes). In 2008, Mustoes merged with a leading PR agency Geronimo to form Kindred, the first fully integrated PR & advertising agency. Nick subsequently led an MBO of Kindred in 2010. Always with a keen interest in business, he backed start-up companies ranging from Hall & Partners (research), ABC Connection (on-line publishing) to Caravell (industrial refrigeration MBO). He is Chairman of Kempton Park Racecourse, a trustee of charity Starlight Children's Foundation and a non-executive director of Hub Capital (corporate finance). Nick is the Senior Independent Director providing an alternative contact for both Directors and shareholders.

Adam Reynolds – Non-Executive Director

Adam is a former stockbroker that specialised in corporate finance. In 2000, he set up Hansard Group plc which was admitted to AIM in 2001. Through a reverse takeover, this became First Africa Oil and Gas plc, one of the most successful listings on AIM in 2005. Since then Adam has built, rescued and re-financed a number of AIM companies including Plectrum plc which was sold to Cairn Energy in 2007, Curidium plc which was acquired by Avacta plc, International Brand Licensing the owner of the Admiral sportswear brand, which has become EKF Diagnostics Holdings plc and Medavinci plc which is now Orogen Gold plc. He is currently a non-executive director of EKF Diagnostics Holdings plc and Chairman of Orogen Gold plc, Hubco Investments plc and Autoclenz Limited.

Dr Charles Roberts – Non-Executive Director

Charles is CEO of Loxbridge Research LLP, a venture pilot investment company specialising in the healthcare and technology sector. He is also CEO of Altermune LLC, working with Nobel Laureate Kary Mullis (inventor of PCR). Charles began his career as a doctor in the UK and worked on drug trials for large pharmaceutical companies, having studied medicine and psychology at University of Dundee, University College London and the University of Oxford.

Senior management team

Name	Position
Nick Claxton	Chief Commercial Officer
Dr Mike Risley	Chief Development Officer

Source: Company reports

Company history

For many years, it has been known that small amounts of fetal DNA leak into and circulate with maternal blood. Zoragen was founded in 2007 in Cambridge to investigate whether this circulating fetal DNA could be used to devise an improved test for the screening of Down's Syndrome in pregnant women.

Premaitha was incorporated in 2013 and on 1st April it entered into an asset purchase agreement with Zoragen Limited whereby it acquired all the technology, IP and assets in return for the 347,000 ordinary shares in Premaitha Ltd (called Premaitha Health Ltd until the AIM reversal).

In June 2014, Premaitha reversed into an AIM-listed cash shell called ViaLogy plc which, together with a concurrent capital increase, resulted in the enlarged entity, renamed Premaitha Health plc, having a net cash position of £8.5m for the development and commercialisation of the IONA test. It should be stressed that the ongoing operations have absolutely no links to the former business known as ViaLogy.

Company history

Date	Event
2007	Zoragen Technologies LLP founded in Cambridge
2013	Incorporation of Premaitha Health Ltd
2013	Premaitha Health acquires Zoragen Technologies and relocates to Manchester
2014	Premaitha Health reverses into ViaLogy plc
2015	The IONA® test gains CE Mark and is launched initially in Europe
2015	Strategic investment by Thermo Fisher Scientific

Source: Company reports

Capital increases

At the time of its reverse takeover of ViaLogy in July 2014, the company raised gross funds of £7.24m via a Placing and Open offer at 11p per share to fund its working capital requirements and obtain CE Mark for its IONA test.

This was followed in July 2015 by a further Placing of shares at 20p to raise £8m in order to accelerate the commercialisation of IONA and to provide further resource for its patent litigation with Illumina. In December 2015, further progress was announced with a strategic investment of £5m from Thermo Fisher.

Capital increases

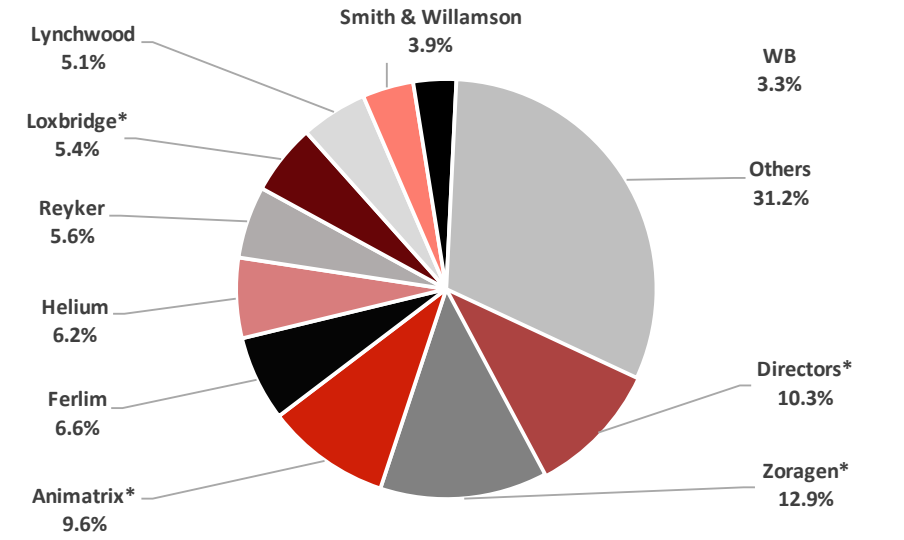
Date	Shares (m)	Price (p)	Raised (£m)	Shares o/s (m)	Valuation (£m)	Comment
				26.89		
Jul-14	95.45	11.0	10.5	122.35	13.5	Consideration shares for reverse take-over
Jul-14	65.81	11.0	7.24	188.16	20.7	Placing & Open offer
Jul-15	40.00	20.0	8.00	228.16	45.6	Placing
Total			**228.16**			

Source: Company reports; Hardman and Co Life Sciences Research

Share capital

The company has 228.16m shares in issue. As a direct consequence of Premaitha's corporate history, Zoragen Biotechnologies, Animatrix and Loxbridge are its largest shareholders and, together with a number of directors and individuals are deemed under AIM rules to be acting as a concert party, currently controlling 39.3% of the issue capital. Directors (some of whom are included in the concert party) own 23.4m shares, or 10.3%.

Major shareholders

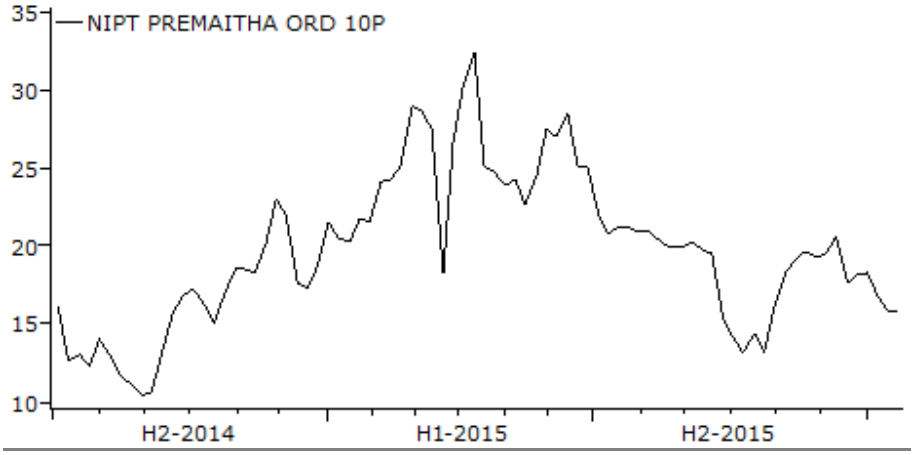


*Part of concert party
Source: Company reports

Share price performance

Overall the stock has performed well since the company reversed into ViaLogy and obtained a stock market listing in 2014. The good news and delivering on its goals enabled the company to raise more capital at a price that was 81% higher than that raised at the time of its listing. However, as can be seen from the chart, it did go through a rapid period of underperformance, which coincided with a member of the concert party selling about 17.5m shares (ca.7.5%). After the stock overhang was removed, the share price quickly recovered. This does highlight the illiquid nature of the stock.

Share price performance since listing on AIM



Source: Fidessa

Thermo Fisher Scientific

Important strategic partnership announced with Thermo Fisher to support further development of the test

Concurrent with Premaitha's interim results (14th December 2015), the company announced that it has signed a long-term investment agreement with one of its core suppliers – Thermo Fisher Scientific (TMO). The DNA library sequencing process within Premaitha's IONA test is run on TMO's Ion Torrent Proton and Ion Torrent Chef sequencing instruments which, unlike some of the reagents, cannot be substituted readily by instruments from an alternative manufacturer. Therefore, there is an inherent link between Premaitha and TMO. The aim of this agreement will be to support the further development of the IONA test through product extensions and to improve the workflow efficiency of the screening process.

Test equipment & workflow

Source: Premaitha Health

TMO in prenatal testing

Thermo Fisher already holds an established leading position in prenatal testing. The biochemical assay used to analyse the blood sample taken as part of the traditional combined test is run extensively on Brahms (wholly-owned subsidiary acquired by TMO in 2009 for 4.5x sales) equipment. Through this test, TMO has links into all relevant clinical testing laboratories already.

Biochemical and genetic testing equipment supplied by TMO

Biochemical (Brahms)

ION Proton (Life Technologies)

Source: Thermo Fisher Scientific

Given this position, TMO then looked to gain access to the newer genetic testing platforms including the using next generation sequencing platforms used in prenatal tests. Its acquisition of Life Technologies Inc in 2014 not only catapulted it to the forefront of such technologies, it also provided the company with the ION Chef and ION Proton equipment that is used in the Premaitha test.

Therefore, through its relationship with Premaitha, Thermo Scientific is intimately associated with the IONA test and competes directly with its major competitor, Illumina, which owns the Verify test.

Strategic partnership

Partnership adds credibility, financial support…and a possible future exit route

As part of the agreement with Premaitha, TMO will be investing £5.0m into Premaitha in the form of a staged long-term loan, together with warrants.

Terms of the agreement

- Staged £5.0m loan to Premaitha attracting a coupon of 6%, with the first tranche of £3.0m received on signing the agreement
- Further milestone-based tranches to be released as required over the next 2-3 years (Hardman estimate)
- The loan is repayable between 14th December 2022 and 13th December 2023, with the option of being repaid earlier
- Warrants for £5.0m over Premaitha ordinary shares at a price of 24.6p per share (a premium of 20% over the price at close of business on day before signature), which expire on the eighth anniversary – 13th December 2023
- On exercise, the warrants would represent 7.1% of the fully diluted share capital of Premaitha

Importance of the agreement

In our opinion, this investment relays a number of important messages:

- Consolidation of the importance of TMO instruments to the IONA test
- Strengthens Premaitha's financial position in its court battle with Illumina
- TMO is unlikely to have made this investment without carrying out its own independent Freedom-to-Operate report, adding further validity to Premaitha's strong defence
- Increasing the ties between the IONA test and TMO's instruments could provide a potential exit strategy

This agreement provides immediate financial support for Premaitha to continue the successful commercialisation of the IONA prenatal screen and to provide resource towards its continual development. In addition, it frees up more financial resources to support Premaitha's litigation costs in proving non-infringement of Illumina's patents and sends a strong message to Illumina that it is no longer dealing with a cash-strapped minnow. From a shareholder's perspective, increasing the ties between Premaitha and Thermo Fisher might provide a long-term exit strategy.

Risks

Investments in relatively small and early stage companies do carry a significant risk and investors must be aware of this fact. In our opinion, the following risks are particularly relevant and any of them could have an impact on commercialisation, and therefore the time to reach cashflow breakeven and profitability.

Dilution risk

The company has sufficient cash to fund its European commercialisation programme and to support distribution arrangements in certain targeted non-European markets. However, if the decision is made to commercialise IONA in the US, both partner(s) and further working capital would be required. Similarly, further extension of the product range, eg into the oncology space, may lead to additional capital requirements. This has the potential to dilute existing investors should they choose not to follow their money.

Regulatory

The company is in a strong position relative to its competitors regarding regulation, given that it has the only commercial product with CE Mark. The situation in the US is more complex and unlicensed tests are performed and commercialised under 'Laboratory Developed Tests' which are under review by the FDA.

Commercialisation

Premaitha is focused initially on the less well established European markets with a CE Marked product which significantly lessens the commercial risk. In contrast, the US market is well developed and dominated by large players with significant financial resources, but the market is large and more ready to accept that the tests can provide reassurance in younger, lower risk, pregnant women.

Litigation

As already seen, the large competitive players will defend vigorously their commercial position, often though court action over patent infringement. This is distracting, time-consuming and costly for small players. However, Premaitha will put up a vigorous defence in the UK and the recent agreement with Thermo Fisher adds credibility to its case and provides substantial financial muscle. However, all litigation carries obvious risks if the claims are successful.

Share liquidity

As with many small cap companies listed on AIM, there can be difficulty in buying and shares in volume. Market makers only guarantee prices in a very small number of shares. The fact that around 50% of the issued capital is controlled by the concert party and directors adds to the illiquid nature of the stock.

Glossary

AIM	Alternative Investment Market of The London Stock Exchange
FDA	Food & Drug Administration
FTO	Freedom-To-Operate
IP	Intellectual property
IVD	*In vitro* diagnostic
IVF	In-vitro fertilisation
KOL	Key opinion leader
KPI	Key performance indicator
LDT	Laboratory Developed Test
MPS	Massively Parallel Sequencing
NGS	Next gene sequencing (DNA technology)
NHS	UK National Health Service
NIPT	Non-invasive prenatal test
ONS	Office of National Statistics
TMO	Thermo Fisher Scientific Inc
USPTO	US Patent & Trademark Office
WIPO	World Intellectual Property Organisation

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The following websites have been regularly visited whilst researching this document:

www.aaaai.org

http://www.ariosadx.com/

www.cdc.gov

http://www.downs-syndrome.org.uk/

ec.europ.eu/eurostat

http://www.illumina.com/?dnr=1

www.ons.gov.uk

http://www.mayoclinic.org/diseases-conditions/down-syndrome/basics/definition/con-20020948

http://www.natera.com/

www.premaithahealth.com

http://www.nhs.uk/Conditions/Downs-syndrome/Pages/Causes.aspx

www.sequenom.com

www.who.int

Notes

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(Disclaimer Version 2 - August 2015)

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