Genetic Signatures
Transforming Molecular Diagnostics

Shareholder Newsletter

SARS-CoV-2 Update

PRODUCT PIPELINE

Measles, Mumps & Rubella
Tick-borne Disease
Dermatophytes

GSS INSTRUMENTATION

Message from the CEO

Dr John Melki

Dear shareholders,

The last 12 months have been transformational for Genetic Signatures, with the company achieving the following milestones:

- Sales have grown by more than 400% on a year-to-date basis (to 31 March 2021) and are already more than double FY2020 full year sales. Significantly, GSS reported its first significant profit ($4.5m) in the 1st half FY2021 and has positive cashflow year to date (as at 31 March).
- Rapidly developed a **3base**™ assay for SARS-CoV-2, the virus that causes COVID-19. This assay complemented the tests that GSS had already developed for the known circulating seasonal coronaviruses.
- We have expanded our manufacturing capacity to meet demand through automation and increased staffing and have now sold kits in all our major target markets – USA, Europe and Australia. The USA and Europe together account for 75% of global testing for infectious diseases and we have an expanding footprint in these markets.
- We have increased the number of Genetic Signatures' branded instruments in use worldwide four-fold compared to 12 months ago. Our growth strategy is to not only increase the number of customers but to also increase the range of tests conducted by current users.
- Our Board was pleased to welcome Dr Neil Gunn as a Non-Executive Director. Dr Gunn brings more than 30 years' experience in the industry and was until recently the President of Roche Sequencing Solutions and prior to that VP of Roche Molecular. His knowledge of the industry will be immensely valuable to our Company.

The year has also seen other milestones achieved or advanced. Among these is registration of another product in Europe with our *EasyScreen*™ STI /Genital Pathogen Detection Kit receiving the CE-IVD mark. Clinical trials have commenced in USA for the *EasyScreen*™ Enteric Protozoan Detection Kit, which is a pre-requisite for FDA clearance of this product.

Genetic Signatures was proud to celebrate its 20th anniversary since founding last month. What started in a laboratory in North Ryde (Sydney) with one staff member in 2001 is now a global supplier of molecular diagnostics kits.

While it is important to reflect on our achievements over the last 12 months, I am very excited about the **new** projects we will be advancing over the next 12 months and beyond. These include a **new** 'sample to result' instrument that will decrease the hands-on time required to run a **3base**™ test, while maintaining our high-throughput workflows as well as **new** and exciting products entering the product development pipeline.

I trust you will enjoy reading the following pages that give further insights into our business and the projects we are working on to further enhance Genetic Signatures' and the **3base**™ advantage.

3base™ is the technology behind Genetic Signatures

3base™ is a platform technology that converts the naturally occurring 4-base microbial genome to 3 bases, and this patented method is a key differentiator between GSS and other molecular diagnostics (MDx) solutions offered by competitors. Of the 4 bases (Adenine, Cytosine, Guanine & Thymine) C is the most unstable and therefore most mutations result from a C-T or T-C conversion. The **3base**™ process converts C into T and thereby greatly simplifies the multiplexing process through reduced sequence variation and by making the sub-types more similar.

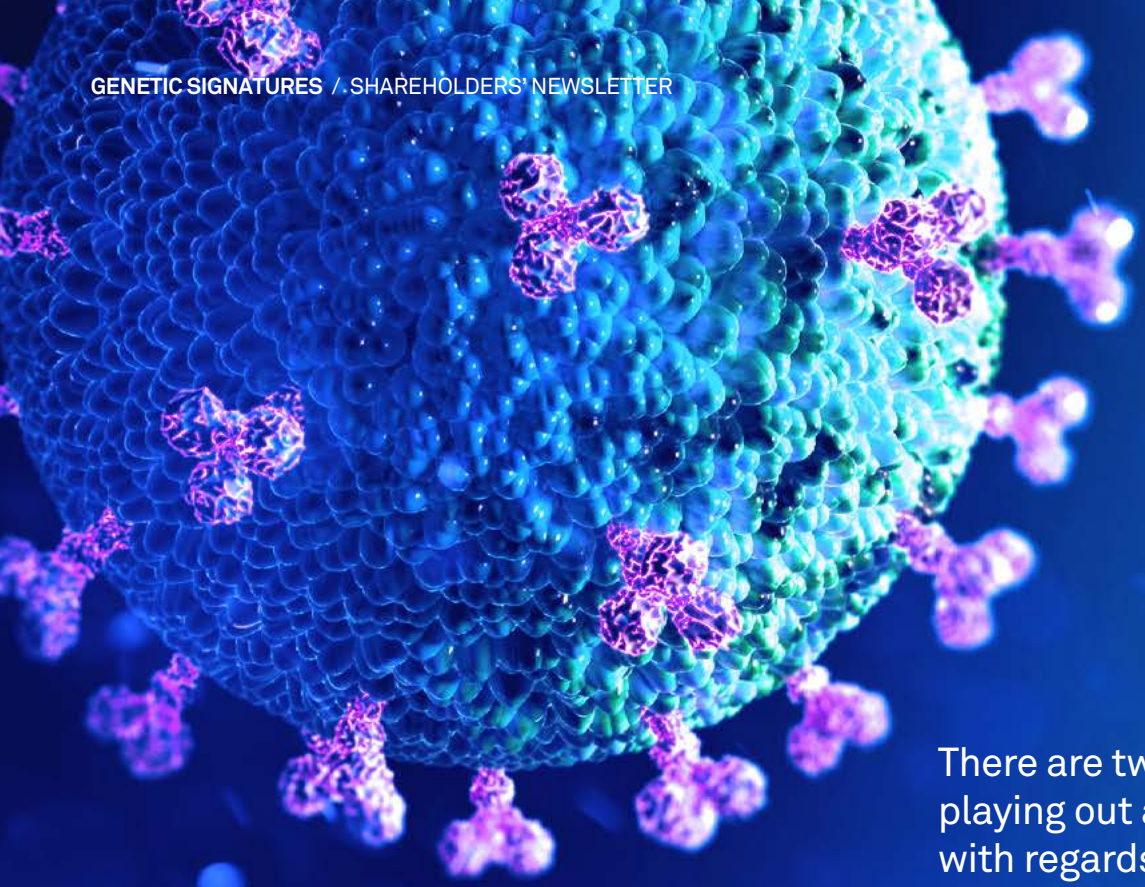
The example below is the sequence for 10 different Human Papilloma (HPV) strains and demonstrates the reduced complexity due to the conversion of the C-T (3 possible combinations with **3base**™ versus 48 combinations in the natural 4-base sequence).

Sequence	Before	After
Seq 1	G A T G G **C** G A **T** A T G G T **T** G A **C** A **C**	G A T G G T G A T A T G G T **T** G A T A T
Seq 2	G A T G G **T** G A **C** A T G G T **A** G A **T** A **C**	G A T G G T G A T A T G G T **A** G A T A T
Seq 3	G A T G G **T** G A **T** A T G G T **G** G A **C** A **C**	G A T G G T G A T A T G G T **G** G A T A T
Seq 4	G A T G G **T** G A **T** A T G G T **A** G A **T** A **T**	G A T G G T G A T A T G G T **A** G A T A T
Seq 5	G A T G G **T** G A **T** A T G G T **G** G A **C** A **C**	G A T G G T G A T A T G G T **G** G A T A T
Seq 6	G A T G G **C** G A **C** A T G G T **T** G A **T** A **T**	G A T G G T G A T A T G G T **T** G A T A T
Seq 7	G A T G G **T** G A **T** A T G G T **G** G A **C** A **C**	G A T G G T G A T A T G G T **G** G A T A T
Seq 8	G A T G G **T** G A **C** A T G G T **A** G A **T** A **C**	G A T G G T G A T A T G G T **A** G A T A T
Seq 9	G A T G G **T** G A **T** A T G G T **A** G A **T** A **C**	G A T G G T G A T A T G G T **A** G A T A T
Seq 10	G A T G G **T** G A **T** A T G G T **G** G A **T** A **C**	G A T G G T G A T A T G G T **G** G A T A T

Consensus

Sequence	G A T G G **Y** G A **Y** A T G G T **D** G A **Y** A **Y**	G A T G G T G A T A T G G T **D** G A T A T
	• 75% homology over 20 bases • **48** possible primer combinations	• 95% homology over 20 bases • **3** possible primer combinations

A good example of the strength of this is with the SARS-CoV-2 virus that has mutated. **3base**™ assays have been tested on the Alpha, Beta, Gamma and Delta SARS-CoV-2 variants; all variants are detected to the same limit of detection as reference SARS CoV 2 virus.



There are two themes playing out around the world with regards the pandemic. Firstly, the virus has mutated and second, the amount of testing being undertaken is rapidly declining in the developed world.

SARS-CoV-2 Update

GSS SARS-CoV-2 assays can identify all known new variants

SARS-CoV-2 variants

Several SARS-CoV-2 variants have been reported widely in the media, and these include the UK variant, South African variant, Brazilian variant, and most recently Indian variants; which have recently been renamed as alpha, beta, gamma and delta variants, respectively. These variants can have increased transmissibility in the community thought to be due to accumulating mutations in the Spike-protein (S) gene, however mutations also occur in all other regions of the virus.

The front-line GSS SARS-CoV-2 assays can identify all new variants. We have confirmed this by extensive analysis of publicly available SARS-CoV-2 sequences, and also physical testing of the variants. All of the abovementioned variants are present in Australia, primarily confined to incoming passenger quarantine facilities. We continuously monitor new sequence information to ensure our assays will still effectively detect all SARS-CoV-2 variants.

The different variants have characteristic patterns of S-gene mutations, although the same mutations can (and continue to) arise independently in different lineages. Thus, some mutations are shared by all variants, and some are specific to a certain variant.

We have developed a suite of assays for a number of these mutations and are currently trialling this kit in Europe as a reflex test, to be performed on SARS-CoV-2-positive samples. This will allow rapid identification of known variants, which will ultimately be confirmed by DNA sequencing by health authorities. We continuously monitor new sequence information to quickly develop assays for new mutations as they arise.

Testing trends

Testing rates in the US have decreased considerably from a peak of up to 700 tests per 100k population at the end of last year to fewer than 200/100k[1], a 70% decline. There are several causes for this ranging from increased vaccine rollout and a sense generally within the community that things are improving so they have become less fearful. The adoption of other technologies such as next generation sequencing (NGS), rapid antigen tests and the modality of testing performed now being more distributed to over the counter or at home tests are also impacting PCR testing rates.

This trend is also being observed in the European & UK markets. However, in the EU/UK markets PCR tests remain steady due to its status as the gold standard for symptomatic testing, and for travellers. While observed rates are lower, the outlook for PCR testing should remain steady until the end of 2021 and may see seasonal uptick in volumes, with combined flu and covid panel tests, as the US heads into the colder months. We also expect this trend in our EU & UK markets.

The ANZ market has remained steady for SARS-CoV-2 testing in the past quarter with some increase from recent surge testing due to outbreaks in Victoria and NSW. As we head into the traditional flu season we expect the increased adoption of syndromic respiratory panel testing. The overall environment in these geographies is suggesting that we are slowly getting back to normality and testing facilities have more capacity to explore other tests other than Covid testing.

[1] https://coronavirus.jhu.edu/testing/individual-states

SARS-CoV-2 Update (Cont.)

3base™ is a molecular PCR test that are the most accurate and therefore considered to be the gold standard.

	MOLECULAR TEST	ANTIGEN TEST	ANTIBODY TEST
Also known as…	**Diagnostic test, viral test, molecular test, nucleic acid amplification test (NAAT), RT-PCR test, LAMP test**	Diagnostic test, viral test, rapid test	Serological test, serology,
How the sample is taken…	**Nasal swabs, either shallow or deep (most tests). Saliva (some tests)**	Nasal or nasopharyngeal swab (most tests	Blood from a fingerstick or vein
How long it takes toget results…	**Less than an hour (at-home tests and some point-of-care locations), same day (some point-of-care locations) or 1-3 days (tests sent to a lab for processing). Some tests may take longer in some locations, depending on testing capacity.**	Some may be very fast (15–30 minutes), depending on the test	Same day (some point-of-care locations) or 1-3 days (tests sent to a laboratory for processing)
Is another test needed…	**Not usually. This type of test is typically highly accurate and usually does not need to be repeated. Some may indicate the need to re-test in certain circumstances.**	Maybe. Positive results are usually highly accurate, but false positives can happen, especially in areas where very few people have the virus. Negative results may need to be confirmed with a molecular test.	Sometimes a second antibody test is needed for accurate results.
What it shows…	**Diagnoses active COVID-19 infection. (Some tests may also diagnose influenza or other respiratory viruses)**	Diagnoses active COVID-19 infection. (Some tests may also diagnose influenza or other respiratory viruses)	Shows if you've been infected by the virus that causes COVID-19 in the past
What it can't do…	**It cannot show if you ever had COVID-19 or were infected with the virus that causes COVID-19 in the past**	It may not detect an early COVID-19 infection. Your health care provider may order a molecular test if your antigen test shows a negative result, but you have symptoms of COVID-19. It also cannot show if you ever had COVID-19 or were	It cannot diagnose COVID-19 at the time of the test or show that you do not have COVID-19

Source: fda.gov/media/140161/download

Progress towards FDA clearance – *EasyScreen*™ Enteric Protozoan Detection Kit

Infectious gastroenteritis remains a worldwide health issue and is the leading killer of children under 5[2]. In the United States there are more than 350 million cases of acute gastroenteritis annually and infections account for 200,000 hospital admissions of children under 5 each year[3]. Early identification of causative pathogens remains a challenge in the clinical laboratory. Traditional diagnosis of infectious gastrointestinal disease can be both incomprehensive and time consuming, two factors effectively addressed by the **3base**™ real-time PCR assays.

Work that was delayed 18 months due to COVID, has now recommenced

Genetic Signatures has identified that testing for Enteric Protozoa (parasites) is an underserved market in the US, with microscopy being used by most laboratories as the primary means to diagnose protozoan infections. An estimated 5.5m samples are tested each year in US[4].

Due to the time involved in undertaking these tests and their limited accuracy many laboratories do not provide the test unless specifically requested. Current molecular tests only identify up to four protozoan pathogens. Conversely, Genetic Signatures *EasyScreen*™ Enteric Protozoan Detection Kit can detect eight of the most common protozoa in a single sample without a loss of accuracy or processing speed.

Testing of clinical samples has commenced at two of three trial sites for the *EasyScreen*™ Enteric Protozoan Detection Kit, with a third site on track to commence in early July 2021. Once all three sites have completed their testing the data will be collated, analysed and a report generated. The data that is also being separately generated to demonstrate the analytical performance characteristics will be combined with the clinical study data to form the 510(k) submission. It is anticipated that the package will be available before the end of CY2021 and that FDA clearance should take 3-6 months.

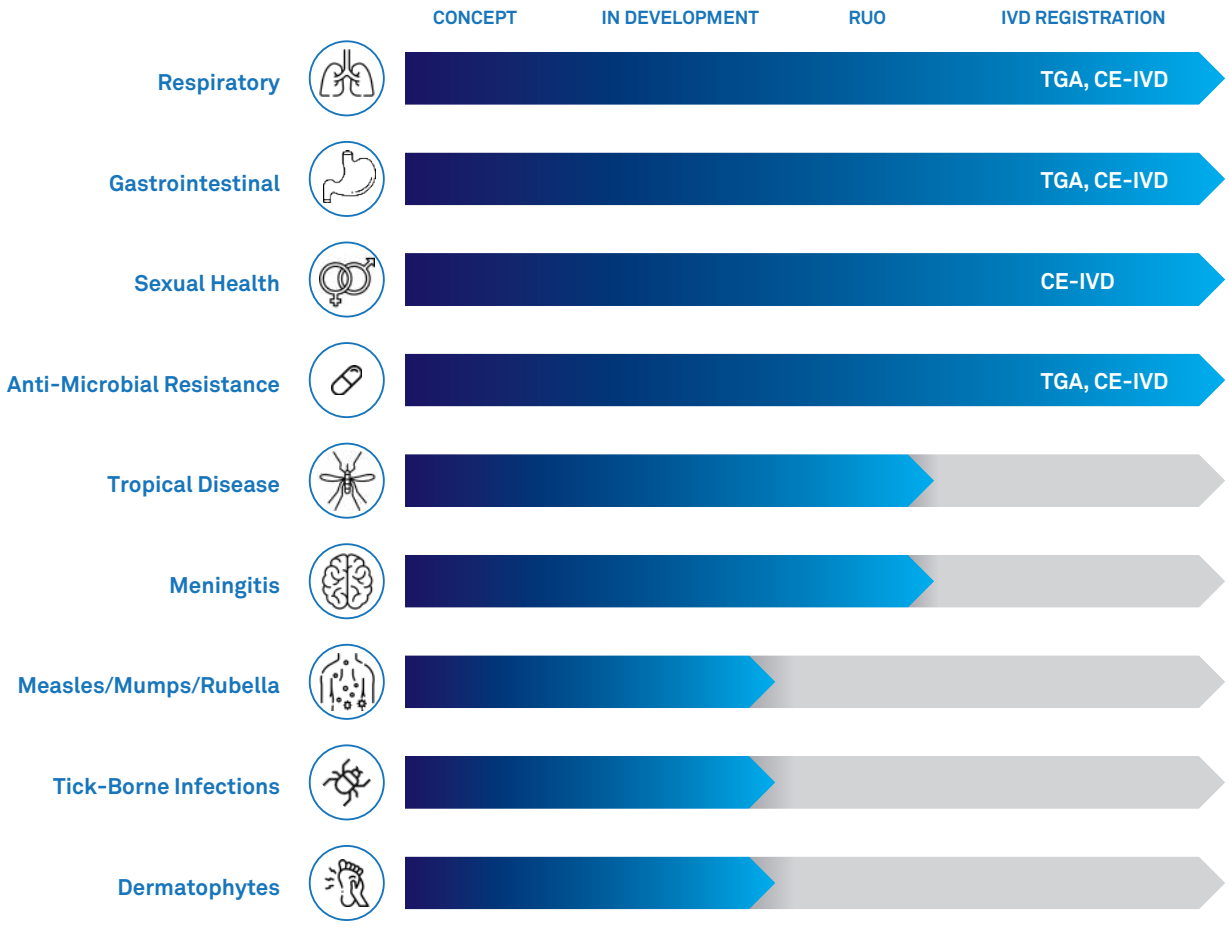
Once the FDA clearance is granted Genetic Signatures is aiming to win up to 40% of the enteric protozoan testing market within five years. The table below demonstrates potential annual revenue at different price points and market shares.

REVENUE PER TEST (US$)	20% MARKET SHARE	30% MARKET SHARE	40% MARKET SHARE
$20	$22.0m	$33.0m	$44.0m
$30	$33.0m	$49.5m	$66.0m
$40	$44.0m	$66.0m	$88.0m

[2] April 2015; Source: Zhang, H., Morrison, S., & Tang, Y. W. (2015). Multiplex polymerase chain reaction tests for detection of pathogens associated with gastroenteritis. Clinics in laboratory medicine, 35(2), 461-486.
[3] August 2020; Source: Sattar, S. B. A., & Singh, S. (2020). Bacterial gastroenteritis.
[4] Bell Potter Securities Estimates (Initiation of Coverage Report) and World Market for Molecular Diagnostics, 5th. Edition (Infectious Disease, Oncology, Blood Screening, Pre-Natal and Other Areas), Kalorama Information, Published: 1/9/2013.

Product Pipeline

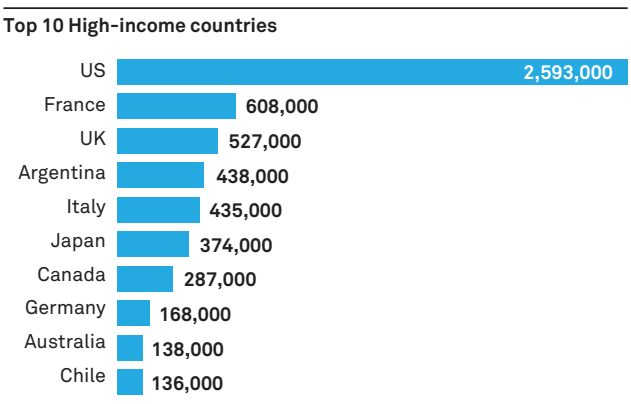
Genetic Signatures has nine product groups, four of which are registered with regulatory authorities and available for sales in at least one jurisdiction around the world. Additionally, two more groupings, tropical diseases and meningitis are available for sale as Research Use Only products. Finally, there are three new products under development, each with market dynamics suggesting **3base**™ solutions will be well received. These products are discussed as follows.



Measles, Mumps & Rubella

Measles, Mumps and Rubella (MMR) are highly contagious viral diseases in which symptoms usually develop 10-18 days after exposure to an infected person and last 7-14 days. Although all three diseases are vaccine preventable, recently there has been a resurgence of disease due to declining vaccine uptake (see graph). In 2017 over 110,000 people died from measles alone. Genetic Signatures has been asked by several hospitals if it was possible for us to produce a rapid multiplexed MMR assay, which we have developed and is now undergoing clinical assessment.

Figure 1. *Children not given first measles vaccine 2010-17*



Source: Unicef

Tick-borne Disease (TBD)

Ticks are a species that can transmit a large number of infectious agents to humans due to their lifecycle. TBD is caused by various species of bacteria, virus and protozoa, which are carried by ticks. Perhaps the most well-known is Lyme disease which is endemic world-wide. Other diseases include Rocky Mountain spotted fever, typhus, Colorado tick fever, anaplasmosis, tularemia, ehrlichiosis and tick-borne encephalitis. Many TBDs cause chronic debilitating diseases that are resistant to therapies and are the cause of significant morbidity worldwide. Very few molecular methods for the diagnosis of TBD exist thus Genetic Signatures has embarked on a new program to design an entirely novel way to identify all agents of TBD rapidly and sensitively from clinical samples to help diagnose these neglected pathogens.

Figure 2. *Annual cases of Lyme Disease in the US*

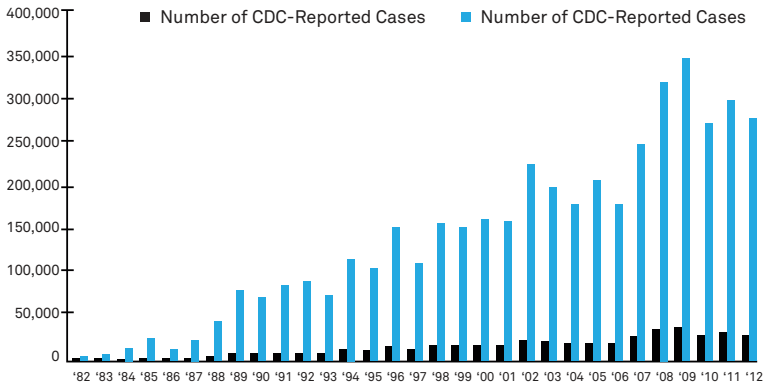
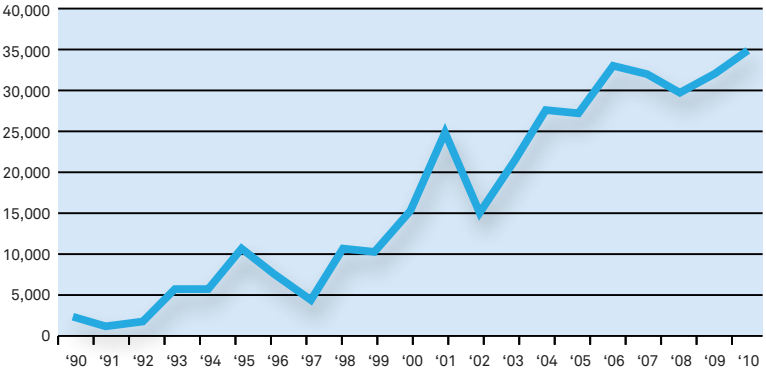


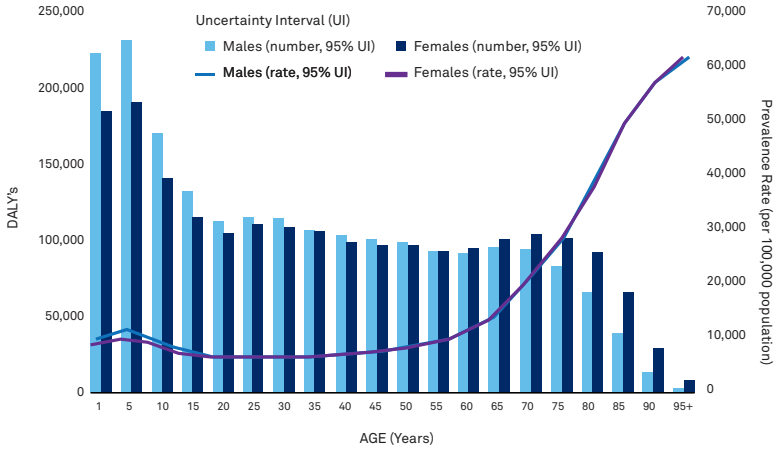
Figure 3. *The increasing prevalence of Lyme disease in Europe from 1990- 2010.*



Dermatophytes

Dermatophytes cause infections of the skin, hair and nails. A well-known example of these fungal skin infections is ringworm or tinea. Fungal growth is usually restricted to the nonliving layer of the skin or nails because of their inability to penetrate viable tissue in healthy people. Infection may become chronic and widespread if the host is immunocompromised. When invasion occurs it elicits a host immune response that can range from mild to severe. Due to the unique **3base™** extraction technology we believe our method will be superior, quicker and have broader coverage than other currently available commercial products.

Figure 4. *Global 2017 fungal skin disease age standardised DALYs per 100,000 people in males and females. DALY, Disability adjusted life year.*



Instrumentation

While GSS diagnostic kits are generally platform agnostic (i.e. can be used on most commercially available instruments), we currently offer four different GSS branded instruments that have been customised to improve processing efficiency while maintaining throughput. These instruments are either sold to customers or are provided under a reagent rental arrangement.

One of our strategic objectives was the commitment to developing a next generation "sample to result" instrument that will be optimised for **3base**™. We have commenced this project and engaged several suitable partners. Through the market research conducted, especially learning from the SARS-CoV-2 pandemic, there are key attributes the market wants to address. It gives GSS a great opportunity to tailor solutions based on market needs. This is an exciting project of significant importance for the long term success of the Company. Further details will be provided as the project progresses.

Image is a concept only

Corporate

Recent research reports and publications concerning GSS:

- 21 May 2021, **Tim Boreham's Crucible: Genetic Signatures,** Biotech Daily https://geneticsignatures.com/au/investors/reports/
- 27 April 2021, **Genetic Signatures (GSS) released its quarterly cash flow statement for 3QFY21 and provided a trading update,** Tanushree Jain, Bell Potter Securities Ltd
- 7 April 2021, **Genetic Signatures sees riches in genes,** Graham Whitcomb, IntelligentInvestor.com.au

Recent Publications

1) Marriott D, Beresford R, Mirdad F, et al. (2021). Concomitant Marked Decline in Prevalence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Other Respiratory Viruses Among Symptomatic Patients Following Public Health Interventions in Australia: Data from St Vincent's Hospital and Associated Screening Clinics, Sydney, NSW. Clin Infect Dis. 2021 May 18;72(10):e649-e651

2) Garae C, Kalo K, Pakoa GJ et al. (2020) Validation of the easyscreen flavivirus dengue alphavirus detection kit based on 3base amplification technology and its application to the 2016/17 Vanuatu dengue outbreak. PLoS One. Jan 17;15(1):e0227550.

3) Del Bianco F, Morotti M, Zannoli S, et al. (2019) Comparison of Four Commercial Screening Assays for the Detection of bla KPC, bla NDM, bla IMP, bla VIM, and bla OXA48 in Rectal Secretion Collected by Swabs. Microorganisms. Dec 16;7(12):704

4) G. Dirani, S. Zannoli, E. Paesini, et al. (2019). *Easyscreen*™ Enteric Protozoa Assay For The Detection Of Intestinal Parasites: A Retrospective Bi-Center Study. Journal of Parasitology 105(1) 58–63

5) R. Gough, J. Ellis, D. Stark (2019). Comparison and Recommendations for the use of Dientamoeba fragilis Real-Time PCR assays. Journal of Clinical Microbiology J Clin Microbiol. 57(5):e01466-18.

6) J. Harkness, D. Marriott, J. Ellis, D. Stark (2019). Evaluation of the *Easyscreen*™ Protozoan Detection Kit for the diagnosis of Entamoeba histolytica. Pathology Pathology. 51(4):426-428

7) Starr K, Greninger AL, Makhsous N, et al. Comparison of Three Adenovirus Quantitative PCR Assays with ATCC Reference Strains and Clinical Samples (2019). J Clin Microbiol. Oct 23;57(11):e00735-19

8) D. Stark, D. Marriott R, J. Harkness, et al. (2019). A syndromic approach to screening sexually-transmitted infections using *EasyScreen*™ Multiplex PCR. Poster presentation, ECCMID, 2019.

9) R. Gough, J. Barratt, J. Ellis et al. (2019). Importance of validating RT-PCR methods for Dientamoeba fragilis. Oral presentation at ECCIMD, 2019.

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