

Direct access to same-day-results





Fully Automated Molecular Diagnostics







FAST

ACCURATE

ASV ACCES



"We at Biocartis aim to provide direct access to personalized medicine for patients worldwide by developing fully integrated and broadly applicable molecular diagnostics. Our platform can be used in a wide variety of healthcare settings to enable rapid and high-quality care close to patients"

Rudi Pauwels, Founder Biocartis



The need for improved, standardized and fast diagnostics

Cancer can hit anyone at any time and treatment remains a real challenge. Because cancer doesn't follow rules. It fights back against therapies. It adapts. It changes its path. It does whatever it can to stay ahead of us.

At the advanced edge of oncology, **rapid access** to **accurate data** about relevant cancer mutations and treatment resistance is vital and creates the opportunity for early disease interception^{4,5}, reducing the anxiety while waiting for results and the time before starting the best possible treatment.

Current technologies in molecular oncology are complex, require a lot of hands-on time and are often difficult to implement in the local laboratory. As a consequence, most laboratories do not perform molecular tests in-house, but send them out to specialized centers, where samples are batched in order to optimize costs. ¹⁻³

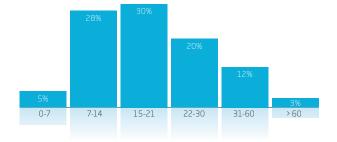
This causes delay to the fast delivery of results, preventing rapid initiation of correct therapy. In the meantime the tumor grows, which is detrimental in case of aggressively growing cancers.

The need for a rapid treatment initiation response towards patients

Fast initiation of immunotherapy or targeted therapy as first-line treatment is crucial for cancer patients, as it increases overall survival rates. 9,10,11,17,22 Timely detection of biomarkers therefore is very important.

Today, turnaround times of reference technologies are on average 18 days, with 14% of patients waiting longer than a month to be able to start treatment. Ninety-five percent of the patients have to wait more than a week in order to receive the biomarker results.⁶

Total turnaround time of reference technologies



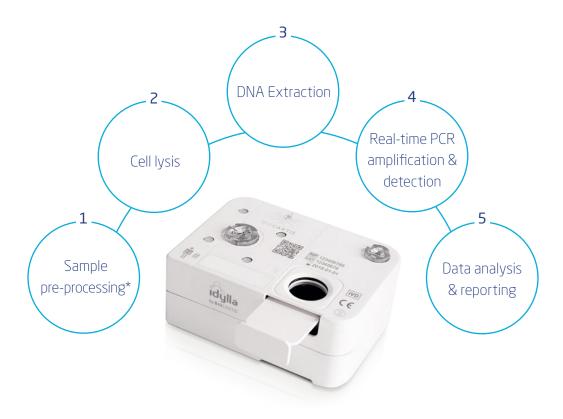
This means that precious time is lost whereas treatment initiation could have been started and unnecessary use of chemotherapy with its side effects could have been avoided.

Idylla[™], the next level in disease interception

IdyllaTM, a **fully automated**, sample-to-result PCR based **molecular diagnostics** system, provides **sameday** results enabling physicians to make **timely decisions** on patients' therapy.

IdyllaTM, can be used with **multiple sample types**, including **solid** and **liquid** biopsies. This flexibility allows use of the system for respectively **diagnosis**, and **research** or possibly future **monitoring** applications.

IdyllaTM, with its **compact scalable design** and **outstanding ease-of-use**, overcomes the traditional barriers of molecular diagnostics, allowing it to be used in virtually **any laboratory setting**.



^{*} e.g. deparaffinization for FFPE tissue samples

Idylla[™] is the first and only molecular diagnostic system that combines



FAST RESULTS

- Less than 2 minutes hands-on time
- Short turnaround time 85 to 150 minutes



ACCURATE RESULTS

- High sensitivity
- Highly standardized technology
- Contamination-controlled design



EASE-OF-USE

- Fully automated sample-to-result process
- Walk-away system (no need for any intervention during the automatic process)
- All reagents integrated in a single cartridge
- Only 1 manual step
- Storage and shipment at room temperature



ACCESSIBLE

 Access on demand - no need for pre-processing or batching



SAMPLE VERSATILITY

• For solid and liquid biopsy



MULTIPLEXING CAPABILITY

- Detection of up to 51 relevant mutations in one cartridge
- Multiple genes and loci detection in one cartridge



CONNECTIVITY

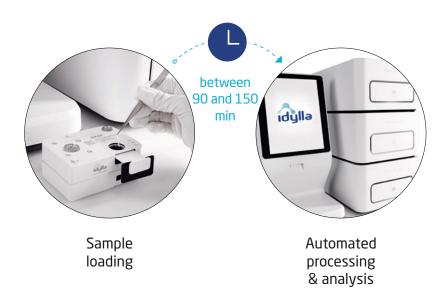
- Remote assistance, monitoring and upgrading
- Bi-directional LIS



The revolutionary Idylla™ workflow

The IdyllaTM system in combination with the IdyllaTM Molecular Oncology Assays differs from other technologies in its outstanding **ease-of-use**, leading to an unsurpassed level of **standardization**, and its **short turnaround time**, allowing immediate access to therapy.

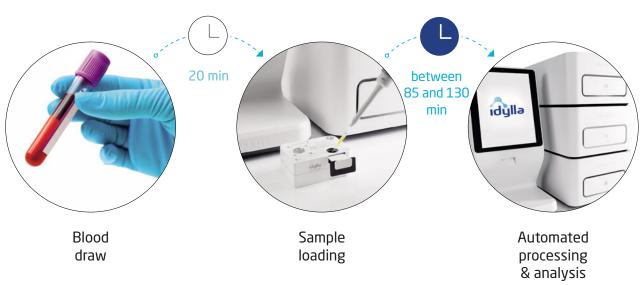
FFPE workflow

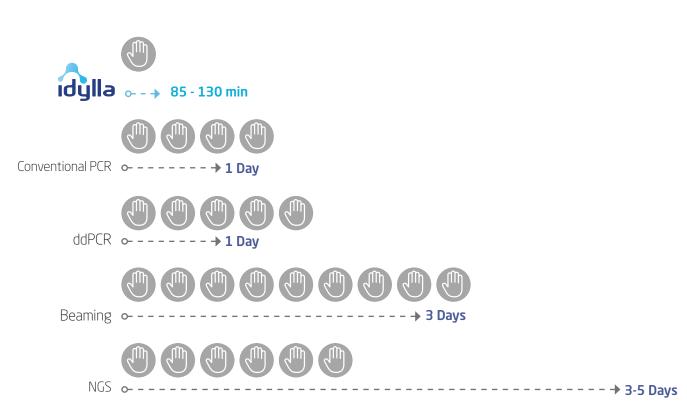






Liquid biopsy workflow





Instruments and consumables



Instruments



Consumables



Lab infrastructure (# of rooms)

1

Other RT-PCR

Instruments



Consumables



Lab infrastructure (# of rooms)

3

Pyrosequencing

Instruments



Consumables



Lab infrastructure (# of rooms)

4

Next generation sequencing

Instruments



Lab infrastructure (# of rooms)

4



Current oncology assays



FFPE in - report out

Diagnostic products (CE IVD)

Idylla™ BRAF Mutation Test

Idylla™ KRAS Mutation Test

Idylla™ NRAS-BRAF Mutation Test

Idylla™ NRAS Mutation Test

Idylla™ EGFR Mutation Test

Research products (RUO)

Idylla™ BRAF Mutation Assay

Idylla™ KRAS Mutation Assay

Idylla™ EGFR Mutation Assay

 $Idylla^{\tiny{\text{TM}}} \ NRAS\text{-}BRAF\text{-}EGFR \ S492R$

Mutation Assay

Plasma in - report out

Diagnostic products (CE IVD)

Idylla™ ctKRAS Mutation Test

Idylla[™] ctNRAS-BRAF Mutation Test

Research products (RUO)

Idylla[™] ctBRAF Mutation Assay

Idylla[™] ctKRAS Mutation Assay

 $Idylla^{\text{TM}}\ ctNRAS\text{-}BRAF\text{-}EGFR\ S492R$

Mutation Assay

Future oncology assay targets



FFPE in - report out

MSI



Plasma in - report out

ctEGFR



Idylla[™] BRAF mutation detection on solid and liquid biopsies



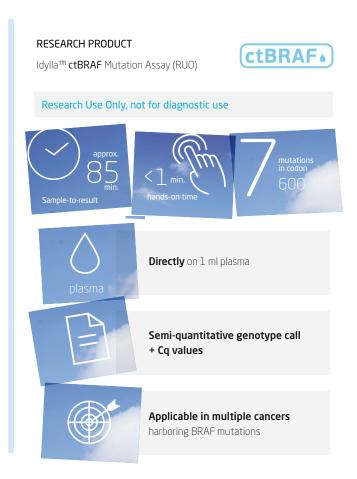
Activating mutations in the *BRAF* gene are observed in about 8% of all cancers⁷ and have been associated with sensitivity and resistance to a number of targeted anti-cancer therapeutics.

Cancers in which *BRAF* mutations are observed include: melanoma, colorectal cancer, thyroid cancer, lung cancer, hairy cell leukemia and ovarian cancer.

BRAF testing is recommended in all patients with metastatic melanoma and metastatic colorectal

cancer (mCRC). About 50% of all metastatic melanoma patients harbor mutations in the *BRAF* gene, making them eligible for BRAF or BRAF/MEK inhibitor therapy.⁸ In mCRC, BRAF mutation status should be assessed alongside the assessment of tumor *RAS* mutational status for prognostic assessment (the presence of a *BRAF* mutation indicates poor prognosis). The prevalence of *BRAF* in mCRC is about 8-15%.⁹

DIAGNOSTIC PRODUCT IdyllaTM BRAF Mutation Test (CE IVD) Diagnostic use | Approx. |



Prof. B. Neyns, M.D., Ph.D Medical Oncology, UZ Brussels, Belgium

"The IdyllaTM system has the potential to allow the start of targeted therapy within a time window of less than 24 hours following the diagnosis of metastasis, thereby saving precious time"



Idylla[™] EGFR mutation detection on solid biopsy



Lung cancer is the most common cancer worldwide, contributing for 13% of all cancer types. 85% of lung cancers are non-small cell lung cancers (NSCLC), of which histologically adenocarcinoma is the most prevalent.

EGFR mutations are mainly observed in lung cancer.

EGFR mutation testing in exons¹⁸⁻²¹ is recommended in all patients with advanced NSCLC of a non-squamous subtype. Activating mutations in the EGFR gene have been associated with sensitivity and resistance to a number of targeted anti-cancer therapeutics.^{11,17}

DIAGNOSTIC PRODUCT

Idylla[™] **EGFR** Mutation Test (CE-IVD)



Exon 19 deletion and exon 21 (L858R, L861), exon 18 (G719X), and exon 20 (S768I) mutations are associated with sensitivity to TKI's. Exon 20 insertion mutation may predict resistance to TKI's. EGFR T790M mutation is the main cause of acquired resistance to TKI therapy and has been reported in about 55% of patients with

disease progression after initial response to 1st or 2nd

The prevalence of *EGFR* mutations in NSCLC adenocarcinomas is 10-15% of Western and up to 50% of Asian patients. Sensitizing *EGFR* mutations are predictive for response to *EGFR* tyrosine kinase inhibitors.^{11,17,21}

Diagnostic use



Prof Giancarlo Troncone

generation TKI's.11,17

University of Napoli Federico II, Naples

"Today, EGFR testing is a cumbersome process and it often takes several weeks before results are analyzed. This may lead to the administration of anti-EGFR therapy as second-line agents, which is less efficient than their use in first-line therapy. The IdyllaTM EGFR Mutation assay technology has the potential to change that: it is a cost-effective solution, ensuring reliable and fast detection of all relevant mutations"

KRAS (ctKRAS.)

Idylla[™] KRAS mutation detection on solid and liquid biopsies

Activating mutations in the *RAS* genes are observed in 9-30% of all cancers and have been associated with sensitivity and resistance to a number of targeted anti-cancer therapeutics.¹² Cancers in which *KRAS* mutations are observed include: colorectal cancer, lung cancer and pancreatic cancer.

According to ESMO⁹, NCCN¹⁴, ASCO¹⁶ and CAP/AMP/ ASCO guidelines¹⁵, genotyping of clinically actionable mutations at a sensitivity of 5% in *RAS* genes exon 2 (codons 12 and 13), exon 3 (codons 59 and 61) and exon 4 (codons 117 and 146) is now mandatory on tumor tissue (either primary or metastasis) of all metastatic colorectal cancers, since the presence of these mutations correlate with the lack of response to certain anti-EGFR antibody therapies⁹. About 46% of all metastatic colorectal tumors harbor mutations in exons 2, 3 and 4 of the *KRAS* gene.¹³

Several studies are ongoing to define the predictive impact of *KRAS* mutations on therapy decision for non-small-cell lung cancer (NSCLC) patients^{18,19,20}. Currently there is evidence that *KRAS* in lung cancer has a prognostic value, indicating poor survival for patients with NSCLC, compared to the absence of *KRAS* mutations.¹¹

Using liquid biopsies for *KRAS* testing is minimally invasive, fast and easy to perform and can be used as an alternative or complement to tissue testing to determine the RAS mutation status at diagnosis.

DIAGNOSTIC PRODUCT

Idylla[™] **KRAS** Mutation Test (CE IVD)



Diagnostic use





Directly on FFPE tissue sections (5-10µm) from metastatic colorectal cancer



Qualitative genotype call



Mutation detection for **baseline treatment**

DIAGNOSTIC PRODUCT

Idylla[™] ctKRAS Mutation Test (CE IVD)



Diagnostic use





Directly on 1 ml plasma from mCRC patients

Qualitative genotype call + Cq values



Mutation detection for **baseline treatment**

Beatriz Bellosillo

Laboratori de Biologia Molecular, Hospital del Mar, Barcelona " Idylla[™] allows very quick results with little hands-on time"

NRAS NRAS - BRAF CtNRAS-BRAF

Idylla[™] NRAS mutation detection on solid and liquid biopsies

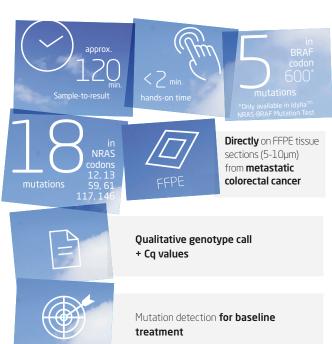
Activating mutations in the *RAS* genes are observed in 9-30% of all cancers and have been associated with sensitivity and resistance to a number of targeted anti-cancer therapeutics. ¹² Cancers in which *NRAS* mutations are observed include colorectal, lung, thyroid cancers and melanoma. According to ESMO⁹, NCCN¹⁴, ASCO¹⁶ and the CAP/AMP/ASCO guidelines¹⁵, genotyping of clinically actionable mutations at a sensitivity of 5% in *RAS* genes exon 2 (codons 12 and 13), exon 3 (codons 59 and 61) and exon 4 (codons 117 and 146) is now mandatory on tumor tissue (either primary or metastasis) of all metastatic colorectal cancers, since the presence of these mutations correlate with the lack of response to certain anti-EGFR antibody therapies⁹.

About 5% of all metastatic colorectal tumors harbor mutations in exons 2, 3 and 4 of the *NRAS* gene.¹³

In metastatic colorectal cancer *BRAF* mutation status should be assessed alongside the assessment of tumor *RAS* mutational status for prognostic assessment (the presence of a *BRAF* mutation indicates poor prognosis).

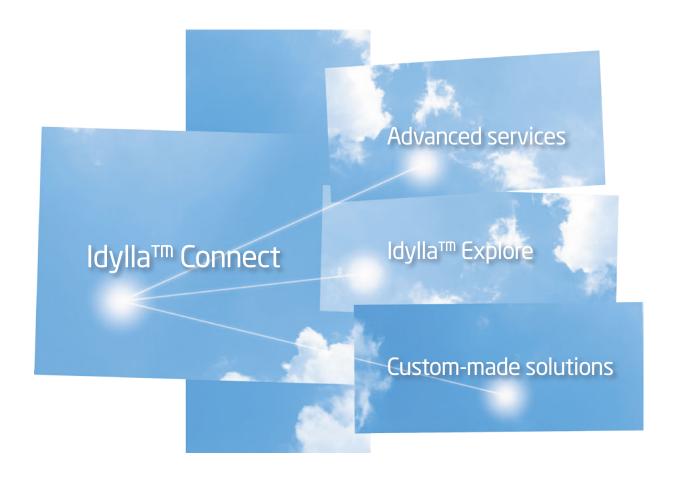
Using liquid biopsies for *NRAS-BRAF* testing is minimally invasive, fast and easy to perform and can be used as an alternative or complement to tissue testing to determine the *RAS* mutation status at diagnosis.







Idylla™ ConnectEngage in the future



- Advanced services to ensure continuity in your laboratory workflow
- Automatic software updates

New releases of assay and console software are sent to your $Idylla^{TM}$ console and can be installed with a single touch on the screen.



Immediate and remote service and support

Idylla[™] system parameters and error logs can be analyzed at anytime and anywhere to ensure swift actions and solutions.



More insight into your data with Idylla™ Explore

Get connected and enjoy **the advantages of IdyllaTM Explore**, a web-based application that allows you to analyze your data by providing

- Visualization of PCR curves from Idylla™Test Results
- Cq values per target
- Direct Access to Console result reports



IdyllaTM Explore can be accessed anywhere and anytime from your PC or tablet through the following link: https://idyllaexplore.biocartis.com

Subscribe today and join the Idylla™ Explore community by sending an email to explore@biocartis.com



Custom-made solutions Biocartis offers personalized solutions that fit your individual needs

- Create a network between different ldyllaTM User sites and share data and knowledge
- Direct access to your data for building your own solution
- Statistical analysis on your obtained data
- Monitoring: Follow-up of your data over time
- Disease surveillance or diagnostic grid: linking of real-time molecular diagnostic test data to geo-location and sample data





Join the investigation

There's a clear need for improved, standardized and fast diagnostics that allow faster initiation of targeted therapy for cancer patients.

IdyllaTM, Biocartis' fully automated molecular diagnostics system, is the first and only molecular diagnostic system that combines unsurpassed ease-of-use, speed and accuracy on multiple sample types. With its **compact**, **scalable design and outstanding ease-of-use**, IdyllaTM overcomes the traditional barriers of molecular diagnostics, allowing it to be used in virtually any laboratory setting.

And by providing same-day-results, IdyllaTM enables physicians to make timely decisions on patients' therapy.

Idylla[™], the next level in disease interception.

Idylla[™] order information

Diagnostic Products (CE-IVD)		
ldylla™ BRAF Mutation Test	6 cartridges/box	Catalog# A0010/6
ldylla™ KRAS Mutation Test	6 cartridges/box	Catalog# A0020/6
ldylla™ NRAS-BRAF Mutation Test	6 cartridges/box	Catalog# A0030/6
ldylla™ NRAS Mutation Test	6 cartridges/box	Catalog# A0040/6
ldylla™ EGFR Mutation Test	6 cartridges/box	Catalog# A0060/6
ldylla™ ctKRAS Mutation Test	6 cartridges/box	Catalog# A0080/6
ldylla™ ctNRAS-BRAF Mutation Test	6 cartridges/box	Catalog# A0090/6
Research Products (RUO)		
ldylla™ BRAF Mutation Assay	6 cartridges/box	Catalog# A0011/6
ldylla™ KRAS Mutation Assay	6 cartridges/box	Catalog# A0021/6
ldylla™ EGFR Mutation Assay	6 cartridges/box	Catalog# A0061/6
ldylla™ NRAS-BRAF-EGFR S492R Mutation Assay	6 cartridges/box	Catalog# A0031/6
ldylla™ ctKRAS Mutation Assay	6 cartridges/box	Catalog# A0081/6
ldylla™ ctBRAF Mutation Assay	6 cartridges/box	Catalog# A0071/6
ldylla™ ctNRAS-BRAF-EGFR S492R Mutation Assay	6 cartridges/box	Catalog# A0091/6
Platform (CE-IVD)		
Idylla ^{rm} Instrument	1 unit	Catalog# P0010
Idylla ^{rm} Console	1 unit	Catalog# P1010

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REFERENCES

- 1. Janku F et al. Oncotarget. 2015; 6(29): 26886—2689.
- 2. Sam SS et al. Pathol Res Pract. 2015. pii: jclinpath-2015—203345.
- 3. Colling R et al. J Clin Pathol. 2015. pii: jclinpath-2015—203345.
- 4. Bratzman SV et al. Expert Rev Mol Diagn. 2015; 15(6): 715—719.
- 5. Siravegna G and Bardelli A. Genome Biol. 2014; 15(8): 449.
- 6. Accès aux tests moléculaires EGFR, RAS et BRAF /Résultats d'une enquête dans 5 régions françaises, appui à la décision, INCa, janvier 2016
- 7. Mutations of the BRAF gene in human cancer. Helen Davies et al; Nature 2002, 417, 949-954
- 8. Clinical Practice Guidelines Cutaneous melanoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 26 (Supplement 5): v126-v132, 2015.
- 9. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Annals of Oncology 0: 1–37, 2016.
- 10. NCCN Clinical Practice Guidelines in Oncology Melanoma Version 3.2016
- 11. NCCN Clinical Practice Guidelines in Oncology NSCLC Version 6.2017
- 12. Adrienne D. Cox et al. Drugging the undruggable RAS: Mission Possible? Nature Reviews Drug Discovery Volume:13,Pages:828–851 Year published:(2014)DOI:doi:10.1038/nrd4389
- 13. Jean-Yves Douillard, M.D., Ph.D., et al. Panitumumab–FOLFOX4 Treatment and RAS Mutations in Colorectal Cancer. N Engl J Med 2013;369:1023-34
- 14. NCCN Clinical Practice Guidelines in Oncology Colon Cancer Version 2.2016
- 15. http://www.amp.org/committees/clinical_practice/CRCOpenComment.cfm
- Allegra C.J. et al. Extended RAS gene mutation testing in metastatic Colorectal Carcinoma to predict response to antiepidermal growth factor receptor monoclonal antibody therapy: American Society of Clinical Oncology Provisional Clinical Opinion Update 2015. Journal of Clinical Oncology 2016; 34(2):179-85
- 17. Novello S. et al. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2016
- 18. ESMO @ ECC 2015: Response to EGFR Agents in Combination With Chemotherapy Demonstrated in Patients with Metastatic Colorectal Cancer of Rare KRAS Molecular Subtype. http://www.esmo.org/Conferences/Past-Conferences/European-Cancer-Congress-2015/News/Response-to-EGFR-Agents-in-Combination-With-Chemotherapy-Demonstrated-in-Patients-with-Metastatic-Colorectal-Cancer-of-Rare-KRAS-Molecular-Subtype. Sept 2015.
- 19. P A Janne et al. BJC 2015. Impact of KRAS codon subtypes from a randomised phase II trial of selumetinib plus docetaxel in KRAS mutant advanced non-small-cell lung cancer.
- 20. Alona Zer et al. J Thor Onco 2015. Pooled Analysis of the Prognostic and Predictive Value of KRAS Mutation Status and Mutation Subtype in Patients with NSCLC Treated with EGFR TKI's.
- 21. Wendy A. Cooper et al. J Thorac Dis 2013; 5 (S5): S479-490. Molecular Biology of lung cancer.
- 22. AACR 2016: 5-Year Survival Rates for Patients With Metastatic Melanoma Treated With Nivolumab Much Higher Than Historical Rates. http://www.ascopost.com/News/39500

NOTICE

Idylla™ BRAF Mutation Test

The MGB Probe contained in the BRAF Mutation Test is covered by applicable US patents and corresponding patents outside the US and is sold under a license from the ELITech Group. The purchase of this product includes a license to use only this amount of product solely for the purchaser's own use solely in the human in vitro diagnostic field (in accordance with applicable FDA and other regulatory requirements) and may not be used for any other commercial use, including without limitation repackaging or resale in any form (including resale by purchasers who are licensed to make and sell kits for use in the 5' Nuclease Process). No right under any other patent claim or for any other use is conveyed expressly, by implication, or by estoppel. Corresponding products conveying rights for use in all other fields may be obtained from Life Technologies under a separate catalog number. For information on obtaining additional rights, please contact outlicensing@lifetech.com or Out Licensing, Life Technologies Corporation, 5791 Van Allen Way, Carlsbad, California 92008.

Idylla™ BRAF Mutation Assay and Idylla™ ctBRAF Mutation Assay

The MGB Probe contained in the IdyllaTM BRAF Mutation Assay and in the IdyllaTM ctBRAF Mutation Assay is covered by applicable US patents and corresponding patents outside the US and is sold under a license from the ELITech Group. The purchase of this product includes a license to use only this amount of product solely for the purchaser's own research use and may not be used for any other commercial use, including without limitation repackaging or resale in any form (including resale by purchasers who are licensed to make and sell kits for use in the 5' Nuclease Process). No right under any other patent claim or for any other use is conveyed expressly, by implication, or by estoppel. Diagnostic use rights for MGB may be obtained under a separate license from ELItech. Corresponding products conveying commercial and diagnostic use rights for MGB may be obtained from LTC only under a separate agreement. For further information contact outlicensing@ lifetech.com or Out Licensing, Life Technologies Corporation, 5791 Van Allen Way, Carlsbad, California 92008.

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Idylla[™] NRAS Mutation Test, Idylla[™] NRAS-BRAF Mutation Test, Idylla[™] ctNRAS-BRAF Mutation Test, Idylla[™] NRAS-BRAF-EGFR S492R Mutation Assay and Idylla[™] ctNRAS3 Mutation Assay

The IdyllaTM NRAS Mutation Test, IdyllaTM NRAS-BRAF Mutation Test, IdyllaTM NRAS-BRAF-EGFR S492R Mutation Assay, ctNRAS3 Mutation Assay and IdyllaTM ctNRAS-BRAF Mutation Test contain PlexZyme and PlexPrime technology covered by patents granted and pending in certain jurisdictions, which are supplied under licence of SpeeDx Pty Ltd. PlexZyme and Plexprime are trademarks of SpeeDx Pty Ltd. The IdyllaTM NRAS Mutation Test, IdyllaTM NRAS-BRAF Mutation Test and the IdyllaTM NRAS-BRAF-EGFR S492R Mutation Assay contain Hilyte and QXL probes. QXL and Hilyte are licensed pursuant to an agreement with Eurogentec S.A. and these licensed probes can be used solely for the purchaser's own research use. HilyteTM is a trademark of Anaspec, Inc. QXL[®] is a registered trademark of Anaspec, Inc.

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IMPORTANT INFORMATION

Idylla[™] platform, Idylla[™] BRAF Mutation Test, Idylla[™] KRAS Mutation Test, Idylla[™] NRAS-BRAF Mutation Test, Idylla[™] Platform, Idylla[™] BRAF Mutation Test, Idylla[™] CtNRAS-BRAF Mutation Test and Idylla[™] CtRAS Mutation Test are CE-marked IVDs in Europe. Idylla[™] BRAF Mutation Assay, Idylla[™] CtBRAF Mutation Assay, Idylla[™] CtRAS Mutation Assay, Idylla[™] KRAS Mutation Assay, Idylla[™] CtRAS Mutation Assay, Idylla[™] CtRAS Mutation Assay, Idylla[™] CtRAS Mutation Assay, Idylla[™] CtRAS Mutation Assay are available for Research Use Only, not for use in diagnostic procedures. Idylla[™] MSI Assay and Idylla[™] CtEGFR Mutation Assay are under development.

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NOTES		

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