

## Test Result Report

PATIENT INFORMATION		PHYSICIAN INFORMATION	
<b>Patient:</b> <First and LastName>		<b>Physician:</b> Dr. <First and LastName>	
<b>Date of Birth:</b> <Mon DD, YYYY>	<b>Gender:</b> <Gender>	<b>Facility:</b> <Ordering Facility Name>	
<b>Tumor:</b> <Tumor Type>	<b>Specimen Type:</b> <Sample Format>	<b>Address:</b> <Street Address, City, State, Postal Code>	
<b>GS Accession No:</b> BDXA#####-XXX	<b>Date of Collection:</b> <Mon DD, YYYY>	<b>Country:</b> <Country Code>	
<b>Date Received:</b> <Mon DD, YYYY>	<b>Date Performed   Reported:</b> <Mon DD, YYYY>	<b>Phone:</b> <Phone Number>	<b>Fax:</b> <Fax Number>

### GENESTRAT® GENOMIC TEST RESULTS

Test	Variant	Results
<b>EGFR Sensitizing</b>	Exon 19 ΔE746-A750	<b>POSITIVE</b>
	Exon 21 L858R	Negative
	Exon 18 G719A, G719C, G719S   Exon 20 S768L   Exon 21 L861Q	Negative
<b>EGFR Resistance</b>	Exon 20 T790M	Negative
<b>ALK Fusions</b>	EML4	Negative
<b>ROS1 Fusions</b>	CD74   SDC4   SLC34A2   EZR   TPM3	Negative
<b>RET Fusions</b>	KIF5B   CCDC6   TRIM33	Negative
<b>KRAS Mutations</b>	G12C	Negative
	G12D	Negative
	G12V	Negative
<b>BRAF Mutation</b>	V600E	Negative

#### INTERPRETATION OF RESULTS

**EGFR | ALK | ROS1\* | RET\* | KRAS | BRAF**

**Positive:**

Presence of 2 or more copies of the variant

**Negative:**

Presence of fewer than 2 copies of the variant

**Quantity Not Sufficient (QNS):**

Test performed, and results not definitive — due to lack of sufficient amount of nucleic acid. No bill will be submitted for this gene.

Redraw recommended

**Test Not Performed (TNP)**

\* For a Positive Result, presence of 10 or more copies of the variant

\* For a Negative Result, presence of fewer than 10 copies of the variant

**Donald Joe Chaffin, M.D.**  
 CAP Accredited CLIA Laboratory Director

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**GENESTRAT® TREATMENT IMPLICATIONS**
**Available Mutations**
**EGFR Sensitizing**

Exon 19 ΔE746–A750 | Exon 21 L858R

Exon 18 G719A, G719C, G719S | Exon 20 S768I | Exon 21 L861Q

**EGFR Resistance**

Exon 20 T790M

**ALK Fusions**

EML4

**ROS1 Fusions**

CD74 | SDC4 | SLC34A2 | EZR | TPM3

**RET Fusions**

KIF5B | CCDC6 | TRIM33

**KRAS Mutations**

G12C | G12D | G12V

**BRAF Mutation**

V600E

**Treatment Implications for Non-Small Cell Lung Cancer<sup>1-14</sup>**

May benefit from treatment with osimertinib, afatinib, erlotinib, gefitinib or dacomitinib

May benefit from treatment with afatinib

May benefit from treatment with osimertinib if previously treated with 1st or 2nd generation EGFR-TKIs

May benefit from treatment with alectinib, brigatinib, ceritinib, crizotinib or lorlatinib

May benefit from treatment with crizotinib, ceritinib or lorlatinib

May benefit from treatment with cabozantinib or vandetinib

KRAS mutations are associated with poorer prognosis

May benefit from dabrafenib + trametinib, vemurafenib or dabrafenib

**GENESTRAT® ANALYSIS DESCRIPTION:**

GeneStrat® genomic testing is a laboratory test service that determines the presence of somatic genetic variants in circulating nucleic acids (DNA and RNA) from the plasma of patients with lung cancer using ddPCR (Droplet Digital™ Polymerase Chain Reaction)<sup>15,16</sup>. In the ddPCR process, a patient sample is dispersed in an emulsion so that individual nucleic acid molecules are isolated. After amplification, nucleic acids are quantified by counting the emulsion that contains PCR end-product, or positive reactions<sup>17</sup>. GeneStrat is a genomic approach to detection of insertion, deletions and point mutations<sup>15</sup>, as well as fusion products<sup>16,17,18,19,20</sup>.

GeneStrat solely reports the presence or absence of certain, limited genomic alterations which may be useful for physicians when considering different therapeutic options. The mutations detected using GeneStrat account for a large proportion of variants found in NSCLC, including EGFR (89% coverage)<sup>21</sup>, ALK (78%)<sup>17</sup>, ROS1 (88%)<sup>22</sup>, RET (99%)<sup>22</sup>, KRAS (78%)<sup>22</sup>, and BRAF (54%)<sup>22</sup>. Accordingly, results are adjunctive to the ordering physician's workup and should be evaluated by a qualified healthcare professional in combination with the patient's clinical history, other diagnostic tests, and clinicopathological factors. For patients that test negative for all mutations, tissue biopsy can be considered. Any questions regarding the use of the GeneStrat test or interpretation of the test results should be directed to Biodesix Customer Care at 1.866.432.5930.

**REFERENCES:**

1. Tagrisso (osimertinib), AstraZeneca Pharmaceuticals, LP, Wilmington, DE, USA.
2. Gilotrif (afatinib), Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA.
3. Tarceva (erlotinib), Astellas Oncology Inc., Northbrook, IL, USA.
4. Iressa (gefitinib), AstraZeneca Pharmaceuticals, LP, Wilmington, DE, USA.
5. Vizimpro (dacomitinib), Pfizer Inc., New York, NY, USA.
6. Alecensa (alectinib), Genentech, Inc. A Member of the Roche Group, South San Francisco, CA, USA.
7. Alunbrig (brigatinib), Takeda Oncology, Cambridge, MA, USA.
8. Zykadia (ceritinib), Novartis Pharmaceuticals Corporation East Hanover, NJ, USA.
9. Xalkori (crizotinib), Pfizer Inc., New York, NY, USA.
10. Lorbrina (lorlatinib), Pfizer Inc., New York, NY, USA.
11. Drilon A, et al. Response to cabozantinib in patients with RET fusion-positive lung adenocarcinomas. *Cancer Discov* 2013; 3:630–635.
12. Drilon A, et al. Cabozantinib in patients with RET-rearranged NSCLC: an open-label, single-centre, phase 2, single-arm trial. *Lancet Oncol* 2016; 17:1653–1660.
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15. Vogelstein B, Kinzler KW. Digital PCR. *PNAS* 1999; 96(16):9236–9241.
16. Mellert H, Foreman T, Jackson L, Maar D, Thurston S, Koch K, Weaver A, Cooper S, Dupuis N, Sathyanarayana UG, Greer J, Hahn W, Shelton D, Stonemetz P, Pestano GA: Development and Clinical Utility of a Blood-based Test Service for the Rapid Identification of Actionable Mutations in NSCLC *Journal of Molecular Diagnostics* 2017.
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18. Mellert, et al. A Blood-based Test for the Detection of ROS1 and RET Fusion Transcripts from Circulating Ribonucleic Acid using Digital Polymerase Chain Reaction. *J. Vis. Exp.* (134), e57079, doi:10.3791/57079 (2018).
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21. Kobayashi Y, Mitsudomi T. Not all epidermal growth factor receptor mutations in lung cancer are created equal: Perspectives for individualized treatment strategy. *Cancer Sci*. 2016;107(9):1179–1186. doi:10.1111/cas.12996.
22. COSMIC database: v79, released 14-NOV-2016. <http://cancer.sanger.ac.uk/cosmic>

GeneStrat was developed and its performance characteristics were determined by Biodesix, Inc. The Biodesix laboratory meets the requirements for high complexity tests under the Clinical Laboratory Improvement Amendments of 1988, as amended, and its implementing regulations.

By accepting receipt of the GeneStrat Test Result Report or any content derived from it ("GS TRR"), the ordering physician, institution of ordering physician, or any third parties to whom the GS TRR is transferred, agree the GS TRR may only be used for the clinical management of the patient identified in the GS TRR by the ordering physician. Any other use of the GS TRR including, without limitation, correlative studies, diagnostic development, derivative works or other analyses, is expressly prohibited. The results of any unauthorized use of the GS TRR shall belong solely and exclusively to Biodesix, Inc. Additional terms and conditions related to this GS TRR can be found at [www.biodesix.com](http://www.biodesix.com).

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