[redacted]

COLLECTION DATE: [redacted]

SPECIMENS:
1. F/S LEFT UPPER LOBE NODULE
2. STATION 8 LYMPH NODE
3. STATION 10 LYMPH NODE
4. STATION 11 LYMPH NODE
5. LEFT UPPER LOBECTOMY
6. STATION 6 LYMPH NODE
7. STATION 5 LYMPH NODE
8. STATION 7 LYMPH NODE
SEE ADDENDUM

Reason For Addendum #1: Molecular Studies
Reason For Addendum #2: Molecular Studies
Reason For Addendum #3: Biomarker Report

DIAGNOSIS:

1,5. LUNG, LEFT UPPER LOBE: WEDGE RESECTION AND COMPLETION LOBECTOMY
- ADENOCARCINOMA, LEPIDIC PREDOMINANT (2.6 CM), SEE NOTE.
- THE BRONCHIAL AND VASCULAR MARGINS ARE FREE OF TUMOR.
- ONE LYMPH NODE, NEGATIVE FOR CARCINOMA (0/1).

Note: The tumor consists of lepidic (60%), acinar (20%), papillary (10%) and micropapillary (10%) components, shows mucinous features and measures 2.6 cm in greatest dimension microscopically. Material will be sent to an outside laboratory for mutational studies and the results will be reported in addenda.

2. LYMPH NODE, LEVEL 8: BIOPSY
- TWO LYMPH NODES, NEGATIVE FOR CARCINOMA (0/2).

3. LYMPH NODE, LEVEL 10: BIOPSY
- ONE LYMPH NODE, NEGATIVE FOR CARCINOMA (0/1).

4. LYMPH NODE, LEVEL 11: BIOPSY
- ONE LYMPH NODE, NEGATIVE FOR CARCINOMA (0/1).

6. LYMPH NODE, LEVEL 6: BIOPSY

- FOUR LYMPH NODES, NEGATIVE FOR CARCINOMA (0/4).

7. LYMPH NODE, LEVEL 5: BIOPSY
- TWO LYMPH NODES, NEGATIVE FOR CARCINOMA (0/2).

8. LYMPH NODE, LEVEL 7: BIOPSY
- FIBROADIPOSE TISSUE WITH LYMPHOID AGGREGATE, NEGATIVE FOR CARCINOMA.

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8: STATION 7 LYMPH NODE

LUNG: Resection
SPECIMEN
Specimen: Lobe(s) of lung (specify)
LEFT UPPER LOBE
Procedure: Lobectomy
Specimen Integrity: Disrupted
Specimen Laterality: Left
Tumor Site: Upper lobe
Tumor Focality: Unifocal
TUMOR
Histologic Type: Adenocarcinoma, mixed subtype
Histologic Grade: G1: Well differentiated
EXTENT
Tumor Size: Greatest dimension (cm)
2.6cm
Additional Dimension (cm): 1.5cm x 1cm
Visceral Pleura Invasion: Not identified
Tumor Extension: Not identified
MARGINS
Bronchial Margin
Bronchial Margin Involvement by Invasive Carcinoma: Uninvolved by invasive carcinoma
Vascular Margin: Uninvolved by invasive carcinoma
ACCESSORY FINDINGS
Lymph-Vascular Invasion: Present
LYMPH NODES
Extranodal Extension: Not identified
STAGE (pTNM)
Primary Tumor (pT):
pT1b: Tumor greater than 2 cm, but 3 cm or less in greatest

dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)
Regional Lymph Nodes (pN)
pN0: No regional lymph node metastasis
Number Examined
11
Number Involved
0
ADDITIONAL NON-TUMOR
Additional Pathologic Finding(s): Emphysema

[redacted]
Pathologist

CLINICAL HISTORY AND PRE - OPERATIVE DIAGNOSIS:
[redacted] ex-smoker (20 pack-years), now with a 2.6 cm LUL nodule.

MACROSCOPIC DESCRIPTION:
The specimen is received in eight parts, each labeled with the patient's name.

1. Part one is received fresh, labeled 'left upper lobe nodule r/o carcinoma'. It consists of a wedge biopsy of the lung measuring 10 x 5 x 2.5 cm. The specimen is received previously incised. Also noted two stapled lines measuring 10 cm and 3.5 cm. The stapled line is shaved and the pleura around the staple is inked black. Also noted on pleura is focal puckering and fibrotic area. Cutting into the specimen reveals a grey-white firm nodule measuring 1.5 x 1.5 x 1 cm. The nodule located is 1.5 cm and 1 cm from both stapled lines. Frozen section performed on the nodule and resubmitted for permanent section. The remainder of the parenchyma is pink-red blotchy and crepitant. Representative sections are submitted.

2. Part two is received in saline, labeled 'station 8 lymph node'. It consists of two pieces of tan and black soft tissue measuring 1.0 x 0.5 x 0.4 cm and 0.6 x 0.3 x 0.2 cm. The specimen is submitted entirely in one cassette.

3. Part three is received in saline, labeled 'station 10 lymph node'. It consists of a piece of black soft tissue measuring 1.2 x 0.6 x 0.3 cm. The specimen is submitted entirely in one cassette.

4. Part four is received in saline, labeled 'station 11 lymph node'. It consists of a piece of black soft tissue measuring 1.0 x 0.3 x 0.2 cm. The specimen is submitted entirely in one cassette.

5. Part five is received fresh, labeled 'left upper lobectomy'. It

consists of a 174 gram upper lobe of the left lung measuring 18 x 8 x 3.7 cm. Along the pleural surface of the lung, is a row of surgical staples extending from the anterior medial apex, obliquely along the anterior lateral pleura for a length of 13.5 cm. The visceral pleura is smooth, reddish purple from subpleural hemorrhage and outlined by black lymphatics. The area surrounding the staples on the anterior surface is inked in green, and the staples are removed revealing dark-red lung parenchyma with a homogeneous cut surface. The lung is serially sectioned and no lesions are grossly seen or palpated. Representative sections are submitted in seven cassettes.

6. Part six is received in saline, labeled 'station 6 lymph node'. It consists of four irregularly-shaped fragments of tan and black soft tissue measuring 1.7 x 1.5 x 0.5 cm in aggregate. The specimen is submitted entirely in one cassette.

7. Part seven is received in saline, labeled 'station 5 lymph node'. It consists of two irregularly-shaped pieces of black soft tissue measuring 0.5 x 0.5 x 0.3 cm and 0.4 x 0.3 x 0.2 cm. The specimen is submitted entirely in one cassette.

8. Part eight is received in saline, labeled 'station 7 lymph node'. It consists of one small piece of black-flecked tan soft tissue measuring 0.3 x 0.2 x 0.2 cm. The specimen is submitted entirely in one cassette.

[redacted]

SUMMARY OF SECTIONS:
1A frozen section control
1B-1E nodule with overlying pleura
1F fibrotic pleura
1G closest stapled line margin to the nodule
2A specimen submitted entirely
3A specimen submitted entirely
4A specimen submitted entirely
5A vascular margin
5B bronchial margin
5C lymph node and additional vascular margin
5D representative of apex
5E representative of hilum
5F representative of mid-lobe
5G representative of lingula
6A specimen submitted entirely
7A specimen submitted entirely
8A specimen submitted entirely

SPECIAL PROCEDURES:

INTRA - OPERATIVE CONSULTATION:

1. F/S LEFT UPPER LOBE NODULE: (Frozen Section)
- Predominantly bronchioloalveolar carcinoma with focus of invasion (acinar pattern)
[redacted]

Intra-Operative Consultation #1 performed by
[redacted]

ADDENDUM # 2 FOR MOLECULAR TESTS:

KRAS and EGFR were sent on [redacted] or patient [redacted] The test is to be performed on tissue from case [redacted] The case report, slides, and blocks for the cited accession number were retrieved from archives. The pathologist whose signature appears below reviewed the original pathology report, examined candidate H&E slides, and selected block 1D appropriate to the specifications of the ordered molecular analysis. x1 H&E and x9 unstained slides were prepared and forwarded to [redacted] where the subject molecular test will be performed. An addendum report will be issued when the results of this molecular test are available.

Addendum #1 performed by
[redacted]

ADDENDUM 2:

[redacted]

RESULTS: Positive for a p.G12A (c.35G>T) mutation in codon 12 of the KRAS gene.

INTERPRETATION: Mutations in the KRAS gene are reported to correlate with poor prognosis and resistance to tyrosine kinase inhibitor therapies in patients with non-small lung cancer.

COMMENT:
KRAS mutations occur in 15-30% of non-small-cell lung cancer (NSCLC) patients and are strongly associated with adenocarcinoma and smoking history.

This assay analyzes codons 12 and 13 in exon 2 of the KRAS gene; based on the current literature, approximately 98% of mutations are expected to occur in these codons. The analytical sensitivity of the assay is approximately 10%; thus mutations present in a low percentage of cells may not be detected.

This test is validated for use in identifying KRAS codon 12 and codon 13 mutations in fresh, frozen, or formalin-fixed paraffin embedded tissue. In particular the test performance has been established in samples of colorectal cancer and non-small cell lung carcinoma which harbor these mutations, although several other tissues are also known to harbor KRAS mutations (e.g. tumors of pancreas, bile duct, ovary, appendix, etc.).

METHOD/LIMITATION:

Tissue sections are reviewed by a pathologist and relevant tumor is selected for analysis. DNA is isolated from the sample, quantified and amplified by polymerase chain reaction (PCR) using primers to exon 2 of the KRAS gene. PCR products are subjected to single nucleotide primer extension to detect mutations at codons 12 and 13; primer extension products are analyzed using capillary gel electrophoresis and fluorescence detection. False positive or negative results may occur for reasons that include genetic variants or somatic heterogeneity of the tissue sample.

REFERENCES:

[redacted]

[redacted]

This test was developed and its performance characteristics determined by [redacted] It has not been cleared or approved by the US Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. The laboratory is regulated under the [redacted] as qualified to perform high complexity clinical testing. This particular test is not considered a stand alone test and should be only used in the context of other diagnostic tests or clinical work-up related to treatment decisions.

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[redacted]

Addendum #2 performed by
[redacted]

ADDENDUM 3:

Genzyme Specimen #: [redacted]

EGFR Mutation Analysis

Clinical Data: Adenocarcinoma

RESULTS: No mutation detected

INTERPRETATION: No mutations were identified; however 18-20% of patients with non-small-cell lung cancer and without identifiable mutations are reported to be responsive to EGFR tyrosine kinase inhibitor therapies.

COMMENT: This assay analyzes exons 18-21 of the EGFR tyrosine kinase domain; based on the current literature, the vast majority of mutations are expected to occur in these exons. The analytical sensitivity of the assay is 10-20%, thus mutations present in a low percentage of cells may not be detected.

Most data published to date pertain to gefitinib (Iressa(r)).
Similar data have been seen in studies using erlotinib (Tarceva(r)).

Homozygosity for the frequently occurring sequence change 2361 G>A was identified. The polymorphism is not likely to have clinical significance.

This test is validated for non-small cell lung carcinoma. The clinical significance and utility of this test in other tumor types is unknown.

METHOD:
Tissue sections are reviewed by a pathologist and relevant tumor is selected for analysis. DNA is isolated from the samples, quantified and amplified by polymerase chain reaction (PCR) using primers to exons 18-21 of the EGFR gene. PCR products are analyzed by bi-directional direct DNA sequencing using capillary gel electrophoresis and fluorescence detection. False positive or negative results may occur for reasons that include genetic variants or somatic heterogeneity of the tissue sample.

REFERENCES:
[redacted]

DISCLAIMER:
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Electronically signed by: [redacted]

[redacted]

Addendum #3 performed by
[redacted]
The electronic signature attests that the named Attending Pathologist has evaluated the specimen referred to in the signed section of the report and formulated the diagnosis therein.

This report may include one or more immunohistochemical stain results that use analyte specific reagents.
The tests were developed and their performance characteristics determined by [redacted] Department of Pathology.

They have not been cleared or approved by the US Food and Drug Administration.
The FDA has determined that such clearance or approval is not necessary.