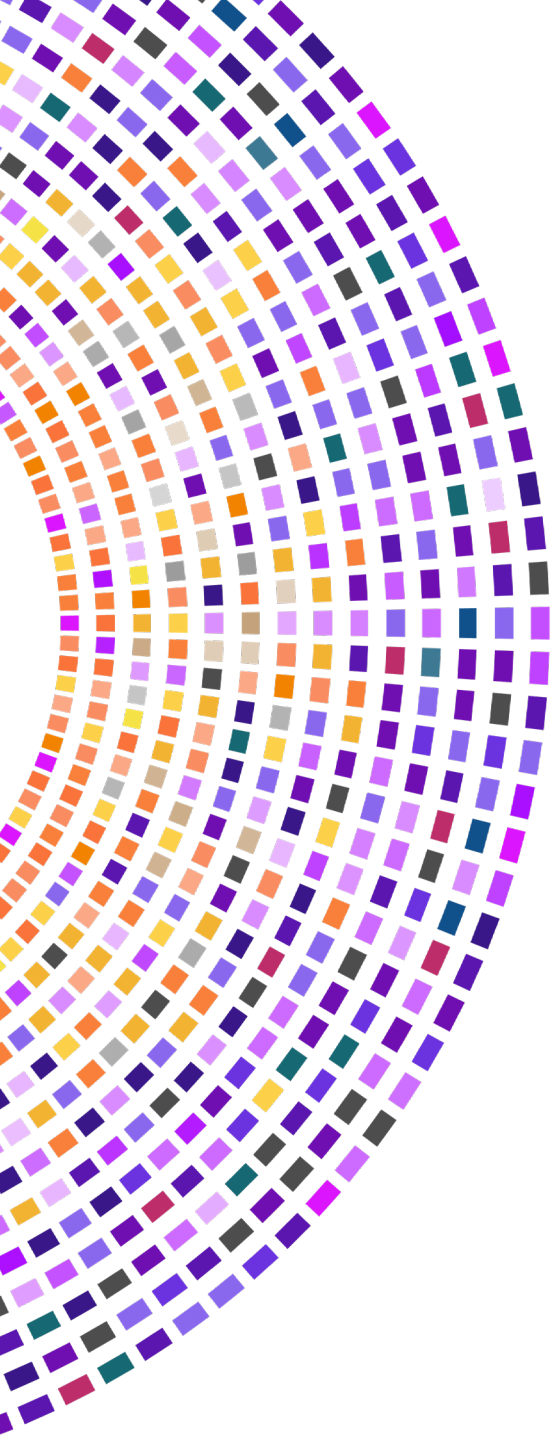


Digital office starter kit

Welcome to Exact Sciences and thank you for your interest in the OncoExTra™ test!

oncoExTra™

by EXACT SCIENCES

oncoExTra™

by EXACT SCIENCES

Welcome!

Dear Valued Client,

Welcome to Exact Sciences and thank you for your interest in the OncoExTra™ test! We look forward to building a meaningful relationship with you and partnering in our mission to help inform life-changing treatment decisions for your patients with advanced-stage cancer.

In this starter kit, you will find all the resources you need to get started with your first OncoExTra order. We strive to provide world-class support every step of the way and we are committed to making it easy for you to:

- Order tests
- Interpret results
- Personalize medicine by applying real-world evidence and guideline recommendations

One of our top priorities at Exact Sciences is to take care of the people we serve. Should you need support beyond the resources in this kit, please contact us so we may assist you further.

Here's to changing lives, together.

Sincerely,

OncoExTra Team
866-662-6897
oncoextra@exactsciences.com

Exact Sciences Corporation
445 N. 5th St, Suite 300 | Phoenix, AZ 85004

EXACT SCIENCES

oncoExTra™

by EXACT SCIENCES

Table of contents

EXACT SCIENCES

oncoExTra™

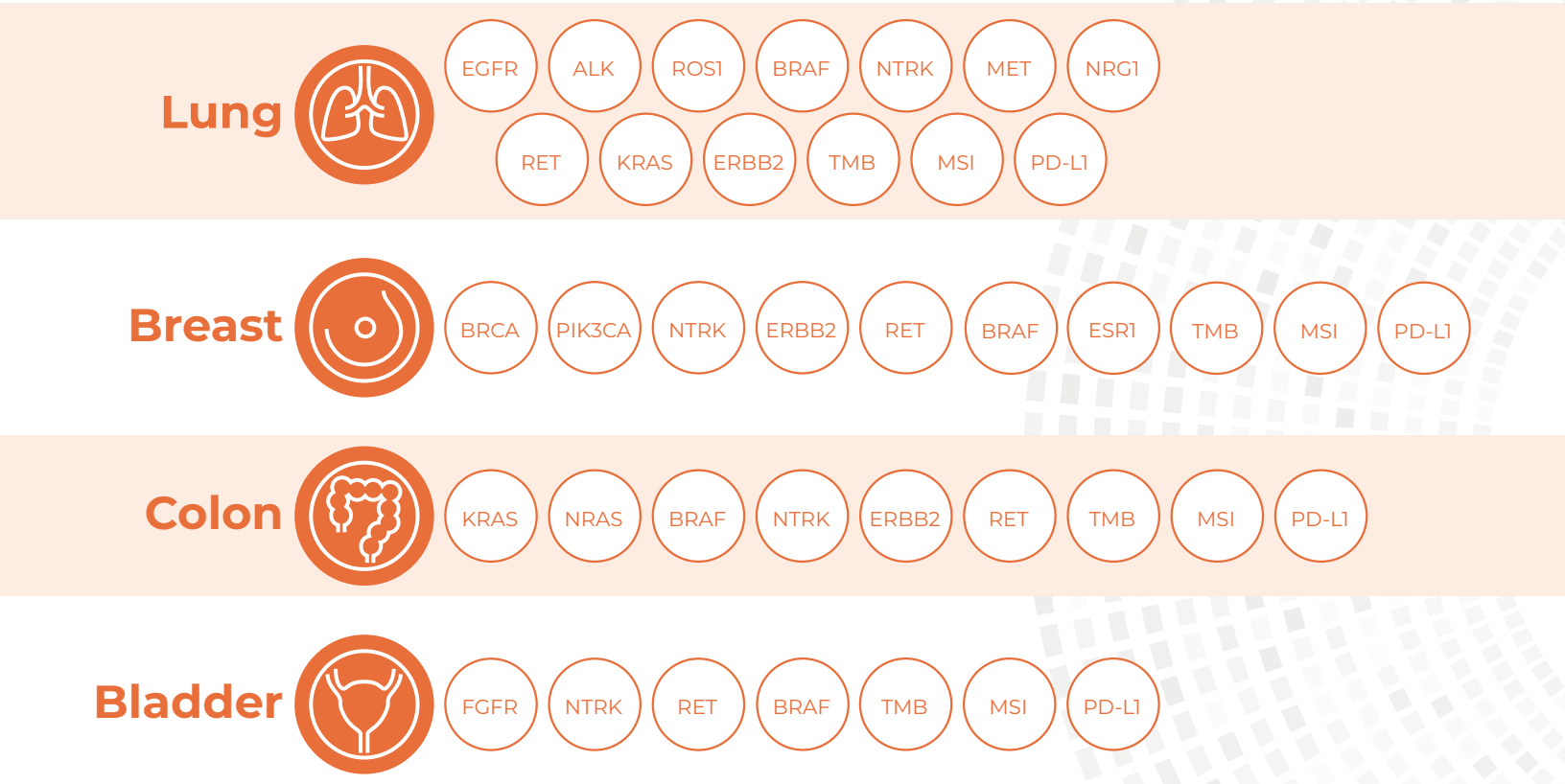
by EXACT SCIENCES

Covered by MEDICARE

Ultra-Comprehensive Genomic Profiling With the OncoExTra™ Test

The OncoExTra test is an ultra-comprehensive genomic profiling assay that incorporates tumor whole exome (DNA) and whole transcriptome (RNA) sequencing with paired tumor-normal analysis to identify alterations/biomarkers in individuals diagnosed with advanced cancers. These insights can help inform targeted therapy options and clinical trials eligibility.

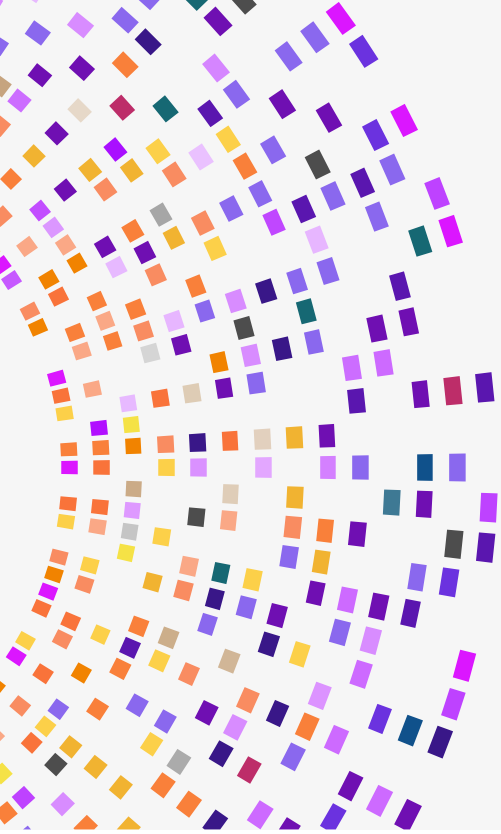
With ~20,000 genes profiled, an assessment of key immuno-oncology signatures (TMB & MSI), clinical trial availability, and Medicare coverage, the OncoExTra test is designed to provide actionable insights to help inform clinical decision making for a breadth of solid tumor types.



In a multicenter retrospective analysis of 1,261 patients tested with the OncoExTra test:[1]

- 75 actionable fusions were detected (5.9%).
- 41% of actionable fusions were supported by RNA sequencing alone and were not detected at the DNA level.
- 100% of RNA-only detected fusions were clinically actionable.

1. White T, Szelinger S, LoBello J, et al. Analytic validation and clinical utilization of the comprehensive genomic profiling test, GEM ExTra®. Oncotarget. 2021;12(8):726-739.



DNA is only half the genomic story

In advanced cancers, ultra-comprehensive genomic profiling requires more than DNA alone.

20% of cancer morbidity occurs in tumors driven by translocations and gene fusions, according to one estimate.[1] Many of these variants are actionable and may be missed by DNA panel-based testing.[2,3]

Panel-based and hotspot testing could be missing actionable variants[2,3]

	DNA	RNA	Paired Tumor-Normal Match
Hotspot DNA	✓		
Hotspot RNA		✓	
Comprehensive genomic profiling (Fixed-panel DNA sequencing)	✓		
OncoExTra™ (whole-exome DNA sequencing + whole-transcriptome RNA sequencing)	✓	✓	✓

WES (DNA): Allows for comprehensive analysis of all protein-coding genes in a sample

WTS (RNA): Allows the identification of transcript variants and fusion genes that may be undetectable through conventional CGP tests, which only employ DNA analysis

DNA+RNA is the natural evolution of CGP,
exposing all variants and leading to the most personalized care[4,5]

More variants, more actionability with **OncoExTra™**

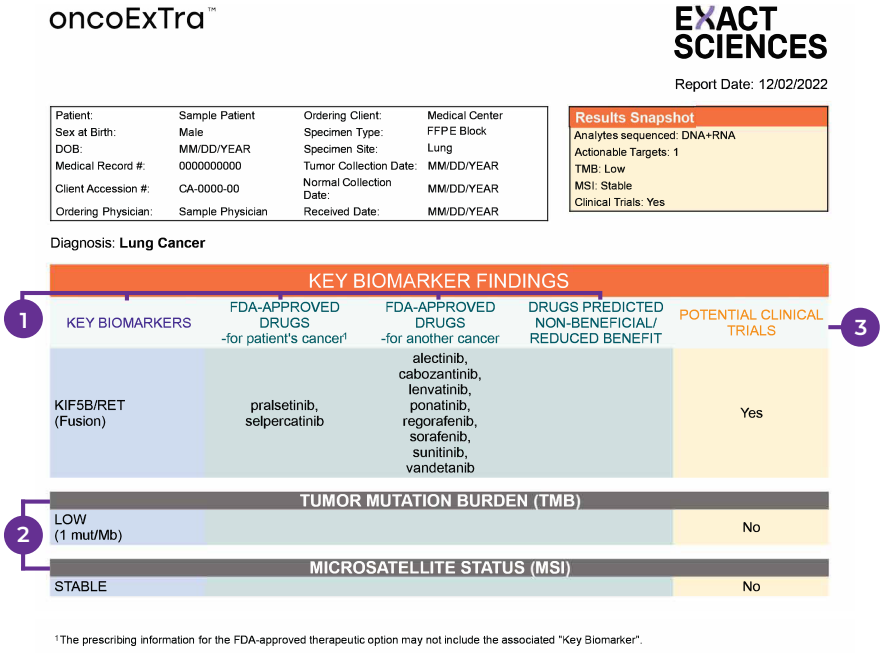
A DNA+RNA profiling test for solid tumors[6] that offers:

- Interrogation of nearly 20K genes
- 98.8% sensitivity / >99.9% specificity
- Tumor and normal-matched sequencing
- Optional immunohistochemical (IHC) panels/single stains for added detail

Clinically proven in a study[6]:

41% of fusions detected at the RNA level alone*

Provide at least 1 clinically actionable variant on 83.9% of reports*†



oncoExTra™

EXACT SCIENCES

Report Date: 12/02/2022

Patient:	Sample Patient	Ordering Client:	Medical Center
Sex at Birth:	Male	Specimen Type:	FFPE Block
DOB:	MM/DD/YEAR	Specimen Site:	Lung
Medical Record #:	0000000000	Tumor Collection Date:	MM/DD/YEAR
Client Accession #:	CA-0000-00	Normal Collection Date:	MM/DD/YEAR
Ordering Physician:	Sample Physician	Received Date:	MM/DD/YEAR

Results Snapshot
Analytes sequenced: DNA+RNA
Actionable Targets: 1
TMB: Low
MSI: Stable
Clinical Trials: Yes

Diagnosis: **Lung Cancer**

KEY BIOMARKER FINDINGS

KEY BIOMARKERS	FDA-APPROVED DRUGS -for patient's cancer[1]	FDA-APPROVED DRUGS -for another cancer	DRUGS PREDICTED NON-BENEFICIAL/ REDUCED BENEFIT	POTENTIAL CLINICAL TRIALS
KIF5B/RET (Fusion)	pralsetinib, selpercatinib	alectinib, cabozantinib, lenvatinib, ponatinib, regorafenib, sorafenib, sunitinib, vandetanib		Yes

TUMOR MUTATION BURDEN (TMB)

LOW (1 mut/Mb)				No

MICROSATELLITE STATUS (MSI)

STABLE				No

[1]The prescribing information for the FDA-approved therapeutic option may not include the associated "Key Biomarker".

Reporting that's easy to interpret and easy to access

1. Mutations and fusions associated with FDA-approved treatments‡
2. Immuno-oncology signatures (TMB/MSI)
3. Clinical trial options

Provider portal:
Results delivered to you within 14 days of receiving sample via a secure and convenient online portal[6]

*Retrospective analysis of 1509 clinical reports, of which 1261 included both DNA and RNA profiling. OncoExTra RNA findings detected variants in 5.9% [75/1261] of samples vs 3.5% [44/1261] in DNA analysis.[6]
†Clinically actionable variants are defined as variants that are associated with available therapies or clinical trial enrollment for a specific somatic variant identified in a patient's tumor.[6]
‡The OncoExTra test is not an FDA-cleared or -approved IVD device or companion diagnostic for the referenced biomarkers and FDA-approved therapies.

References
1. Mitelman F, Johansson B, Mertens F. The impact of translocations and gene fusions on cancer causation. *Nat Rev Cancer*. 2007;7(4):233-245. **2.** Drenner K, Basu GD, Goodman LJ, et al. The value of comprehensive genomic sequencing to maximize the identification of clinically actionable alterations in advanced cancer patients: a case series. *Oncotarget*. 2021;12(18):1836-1847. **3.** Nikanjam M, Okamura R, Barkauskas DA, Kurzrock R. Targeting fusions for improved outcomes in oncology treatment. *Cancer*. 2020;126(6):1315-1321. **4.** Berger MF, Mardis ER. The emerging clinical relevance of genomics in cancer medicine. *Nat Rev Clin Oncol*. 2018;15(6):353-365. **5.** Freedman AN, Klabunde CN, Wiant K, et al. Use of next-generation sequencing tests to guide cancer treatment: results from a nationally representative survey of oncologists in the United States. *JCO Precis Oncol*. 2018;2:1-13. **6.** White T, Szelinger S, LoBello J, et al. Analytic validation and clinical utilization of the comprehensive genomic profiling test, GEM ExTra®. *Oncotarget*. 2021;12(8):726-739.

EXACT SCIENCES

oncoExTra™

by EXACT SCIENCES

Placing your first order

Placing an order is simple.

- Are you an existing Exact Sciences Precision Oncology Customer with portal access?

YES	Submit your first order on our Precision Oncology Provider Portal
NO	Sign up for online ordering today

- Follow the instructions on the following pages to submit your first OncoExTra™ order!

What are the benefits of using the provider portal?

- Place orders online any time
- Assign delegates to place your orders
- Obtain results as soon as they become available
- Retain all test results in once place
- Receive up to date announcements on report enhancements
- Sign supporting forms and documents for orders

Frequently asked questions

How do I know if I'm an existing customer?

If you or any of your delegates have ordered any of the following tests from Exact Sciences, you are an existing customer.

oncotype DX®

What if I haven't signed up for the Precision Oncology Provider Portal?

We encourage you to request portal access today, but if you prefer, you may place an order by fax using our paper order form.

Who can I contact with more questions or for immediate assistance?

Please call Customer Service at:
866-662-6897

EXACT SCIENCES

oncoExTra™

Portal Ordering Guide Checklist

Before you start, have these four items ready:

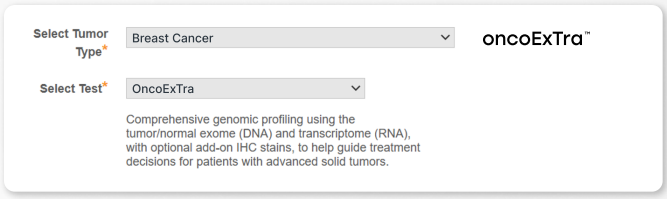
1. Pathology Report
2. Patient Demographic Sheet
3. Front & Back of patient's insurance card
4. Any other molecular results the patient may have

The information presented herein is for illustrative purposes only and does not constitute reimbursement or legal advice. Providers are responsible for submitting accurate and appropriate claims for services and determining medical necessity, the proper site for delivery of any services and submitting appropriate codes, charges, and modifiers for services that are rendered. Payer policies will vary and should be verified prior to treatment for limitations on diagnosis, coding or site of service requirements.
The OncoExTra test is performed by Genomic Health, Inc., a wholly-owned subsidiary of Exact Sciences Corporation.

Submit a New Order

oncoExTra™

- Log onto provider portal - online.genomichealth.com
- Select “Start/Continue Order”.
- Select Tumor Type and Select Test as “**OncoExTra**”.



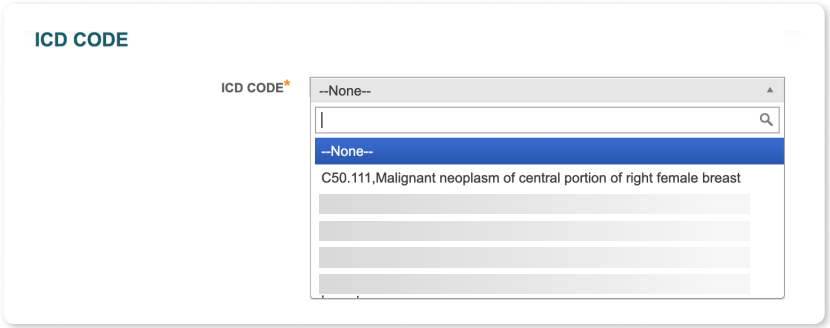
Patient Information

- Select Yes or No does the patient have any of the following:
- Select recurrent, relapse, refractory, advance (stage III/IV) or metastatic cancer.

- Enter patient clinical information.

Billing Information

- Enter patient’s information.
- Select patient’s payment information.
  - For private insurance, use the smart search to select the patient’s payor. If unable to find in the drop down, select “Other” and enter required fields.
- Confirm the ICD code corresponds with the patient’s primary tumor type.



Coding options listed are commonly used codes and are not intended to be an all-inclusive list. Submitting providers should consult relevant manuals for appropriate coding options.

Questions?

Phone:
1-866-662-6897
M-F 5:30AM-5:00 (PST)

Fax:
602-682-5077

Email:
oncoextra@exactsciences.com

Website:
https://precisiononcology.exactsciences.com/contact-us

All fields with “” are required

Physician Information

Ordering Physician Information

- Enter ordering physician information.
- You can update fax and phone numbers for the specific order. You can customize where we send messages and reports.
- If you do not see the correct ordering physician under your desired account, please contact us to update your account settings.

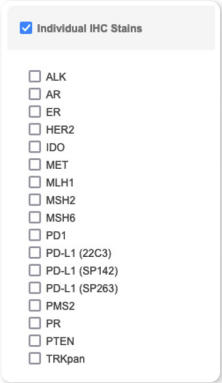
Additonal Report Recipients

- Enter report recipients information.
- Select “Add Recipient” for additional physicians to receive a copy of the report.

Specimen

Testing Options

- Select your testing option: OncoExTra, OncoExTra+ IHC or Individual IHC staining.
  - If you select OncoExTra or OncoExTra full, you may also select Individual IHCs.



- By default, the table is collapsed. When selected, it expands to display all IHCs.
- If the Individual IHCs testing option is selected, at least 1 IHC must be selected.

Specimen - Matched Normal

- Enter date of patients’ blood collection and specimen ID.

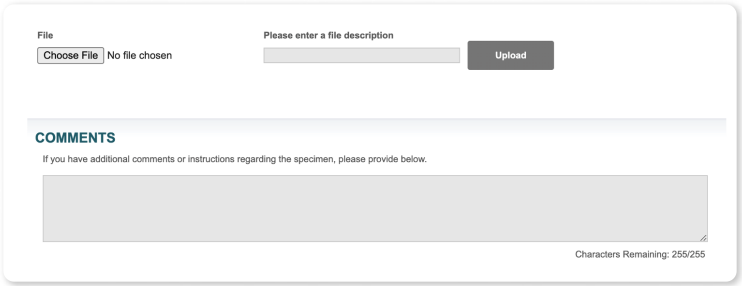
Tips

- The OncoExTra test examines both tumor tissue and a matched-normal blood sample to identify benign mutations, so that treatment can target the most actionable variants.
- Exact Sciences will work directly with the pathology team and treating physician to obtain samples of both solid tumor tissue and matched-normal blood.
- If the pathology account is not in your drop down, add location to the address book to save for future orders.

All fields with “” are required

Medical Documents & Comments

- **Important!** Upload all supporting documents on this tab.
  - Pathology report
  - Clinical progress note
  - Front and back of insurance card
- Enter any additional comments or instructions regarding the specimen.



Review Information

- Verify order information.
- Select “Run Verification” to confirm your patient’s insurance coverage. This may help reduce order processing time.
- Then click “Submit Order”.

There might be pre-billing documents to complete if required under your patient’s insurance before or after you submit a order.

What’s Next?

- **Submit new order** (You are here)
- Pathology lab ships sample
- Exact Sciences recieves samples. Testing begins
- Results are uploaded to portal and faxed to ordering physician

Typically reports are available within 14 days from the date Exact Sciences receives both the tumor sample and matched normal blood sample. Results can be accessed from the provider portal.

For help understanding OncoExTra test results, please contact our Medical team at **medicalsupport@exactsciences.com**

All fields with “” are required

oncoExTra™

by EXACT SCIENCES

Sample Submission Guidelines

Solid Tumor
Specimen Requirements and Shipping Guidelines

	Specimen type	Requirements	Storage and transport
Tumor samples	Paraffin block	Fixed tissue with surface area ≥25 mm^2	Ship overnight with cold pack. Cold pack must be frozen.
	Core needle biopsy	3-5 cores from a single tumor	
	Specimen type	6-10 freshly cut strolls at 10 µm each	
	Unstained slides (USS)	10 (charged, unbaked) from a single tumor, ≥50 µm total + H&E	
	Fresh frozen tissue	5 mm^3	Ship overnight on dry ice
	Minimum tumor content is 20% Send H&E slide or attestation of tumor content for tumor samples along with corresponding pathology report If sending decalcified bone samples in FFPE, use EDTA-based methods—do not use strong acids		
Matched normal matches	Peripheral blood	3-5 mL EDTA, ≥7 days old upon request	• Refrigerate if storing before transport. • Ship overnight with cold pack. Cold pack must be frozen.
IHC testing	Paraffin block	5-10 µm of tissue used per USS	• Refrigerate if storing before transport. • Ship overnight with cold pack. Cold pack must be frozen.
	Unstained slides	2 (charged, unbaked) slides at 4-5 µm per IHC stain 8 (charged, unbaked) slides at 4-5 µm per IHC panel	

EDTA=ethylenediaminetetraacetic acid, FFPE=formalin-fixed, paraffin-embedded.

- Ensure that all primary specimen containers are labeled with 2 unique patient identifiers and collection date
- Testing will not begin until both tumor and matched normal samples are received
- Freeze cold pack included in specimen kit for a minimum of 4 hours before shipping
- Please contact us if you have alternative sample types

EXACT SCIENCES

oncoExTra™

by EXACT SCIENCES

Covered by MEDICARE

A Comprehensive and Easy to Interpret Clinical Report

The OncoExTra™ assay is an **ultra-comprehensive genomic profiling test** that incorporates whole-exome and whole-transcriptome sequencing to identify alterations/biomarkers in patients diagnosed with all types of advanced cancers. These insights can help inform targeted therapy or immunotherapy selection, and clinical trials eligibility.

The OncoExTra Test Provides:

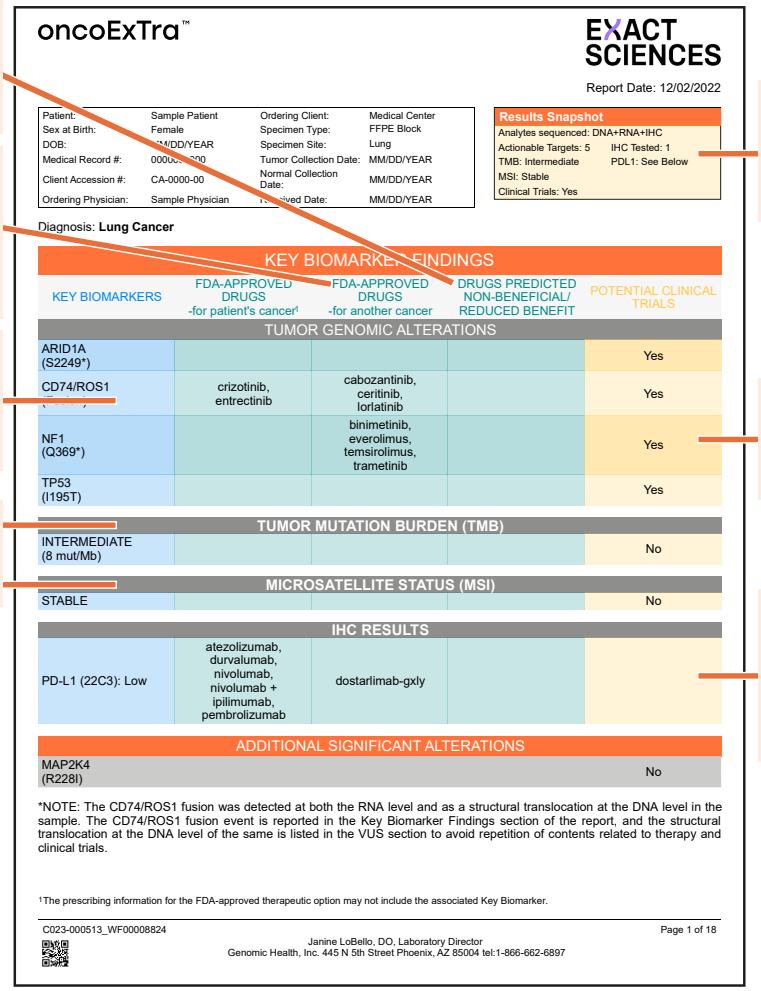
- 3 report types: OncoExTra + IHC, OncoExTra Only, or IHC Only
- Easy to interpret "Results Snapshot" on page 1 of the report
- Color coded sections to help correlate findings

Drugs predicted to have no or reduced benefit as supported by literature

Additional therapeutic options outside of patient's cancer sub-type

Targetable Mutations and Associated Therapies

TMB & MSI Status



oncoExTra™

EXACT SCIENCES

Report Date: 12/02/2022

Patient:	Sample Patient	Ordering Client:	Medical Center
Sex at Birth:	Female	Specimen Type:	FFPE Block
DOB:	MM/DD/YEAR	Specimen Site:	Lung
Medical Record #:	0000[illegible]00	Tumor Collection Date:	MM/DD/YEAR
Client Accession #:	CA-0000-00	Normal Collection Date:	MM/DD/YEAR
Ordering Physician:	Sample Physician	Received Date:	MM/DD/YEAR

Results Snapshot
Analytes sequenced: DNA+RNA+IHC
Actionable Targets: 5 IHC Tested: 1
TMB: Intermediate PDL1: See Below
MSI: Stable
Clinical Trials: Yes

Diagnosis: **Lung Cancer**

KEY BIOMARKER FINDINGS

KEY BIOMARKERS	FDA-APPROVED DRUGS -for patient's cancer[1]	FDA-APPROVED DRUGS -for another cancer	DRUGS PREDICTED NON-BENEFICIAL/ REDUCED BENEFIT	POTENTIAL CLINICAL TRIALS
TUMOR GENOMIC ALTERATIONS				
ARID1A (S2249*)				Yes
CD74/ROS1 [illegible]	crizotinib, entrectinib	cabozantinib, ceritinib, lorlatinib		Yes
NF1 (Q369*)		binimetinib, everolimus, temsirolimus, trametinib		Yes
TP53 (I195T)				Yes
TUMOR MUTATION BURDEN (TMB)				
INTERMEDIATE (8 mut/Mb)				No
MICROSATELLITE STATUS (MSI)				
STABLE				No
IHC RESULTS				
PD-L1 (22C3): Low	atezolizumab, durvalumab, nivolumab, nivolumab + ipilimumab, pembrolizumab	dostarlimab-gxly		
ADDITIONAL SIGNIFICANT ALTERATIONS				
MAP2K4 (R228I)				No

*NOTE: The CD74/ROS1 fusion was detected at both the RNA level and as a structural translocation at the DNA level in the sample. The CD74/ROS1 fusion event is reported in the Key Biomarker Findings section of the report, and the structural translocation at the DNA level of the same is listed in the VUS section to avoid repetition of contents related to therapy and clinical trials.

[1]The prescribing information for the FDA-approved therapeutic option may not include the associated Key Biomarker.

C023-000513_WF00008824 Page 1 of 18

Janine LoBello, DO, Laboratory Director
Genomic Health, Inc. 445 N 5th Street Phoenix, AZ 85004 tel:1-866-662-6897

Snapshot of Key findings

Clinical Trial Options

IHC Results with therapeutic indications

Additional Report Details

Genomic Alteration Detail

Genomic Alteration		Therapeutic Implication	
Alteration:	ARID1A (S2249*)	**Drug**	**Status**
Alteration Type:	Stop Gain	See Clinical Trials Section	
Coordinate:	chr1:27107135		
Allele Frequency:	24%		
Origin:	DNA		
Read Depth:	465		
Location:	20/20		

Drug Evidence Detail

Literature Supporting Therapeutic Implication

Drug	Biomarker	Therapeutic Implication
ceritinib (Zykadia)	CD74/ROS1 (Fusion)	PREDICTED BENEFICIAL

ROS1 rearranged NSCLC patients (n=32) were enrolled in a phase II ceritinib trial. The ORR was 63% with 1 complete response and 19 partial responses. The median duration of response was 10.0 months. The median PFS was 19.3 months and the median OS was not reached at the time of the data cut off.

https://academic.oup.com/annonc/article/27/suppl_6/1205PD/2800071 *(Lim SM et al., Ann Oncol (2016) 27 (suppl_6): 1205PD)*

Clinical Trials

Potential trials based on genomic targets indicated in the OncoExTra Report

Genomic Alterations	Targeted Investigational Agents	Trial IDs
ARID1A (S2249*)	AKT inhibitors: (Afuresertib [GSK2110183], Capivasertib [AZD-5363], Ipatasertib [GDC-0068, RG-7440], Miransertib [ARQ092], ARQ751, MK-2206, Triciribine [TCN-P]), ATR inhibitors: (Berzosertib [M 6620, M6620, VX 970, VX970,	NCT05023655 NCT02264678 NCT02484404 NCT05053971 NCT01582191 NCT03065062

IHC Score Detail

1 IHC Tested

IHC BIOMARKER	IHC Data	Status	Approved By
PD-L1 (22C3)	%TPS: 5-9	Low	Dr. Sample Pathologist (MM/DD/YEAR)

EXACT SCIENCES

EXACT SCIENCES

Genomic Access Program

HELPING PATIENTS ACCESS PRECISION ONCOLOGY PORTFOLIO OF TESTS

Our Commitment to You:

As the world's leading provider of genomic-based diagnostic tests, Exact Sciences is committed to improving cancer treatment decisions and optimizing cancer care. We believe you should have access to the information you need to make confident, informed decisions about your treatment options.

To ensure you can focus on your health, Exact Sciences created the Genomic Access Program (GAP), which helps eligible patients determine payment options. To learn more, contact our Customer Service group by phone at **888-662-6897, option 2.**

Exact Sciences' Precision Oncology portfolio includes tests that apply advanced geno mic science to reveal the unique biology of your individual tumor to help you and your doctor determine the best treatment or management option for you.

How the Genomic Access Program (GAP) Works:

If you have private health insurance, Exact Sciences bills your insurance once testing is complete and we confirm your insurance coverage.[1]

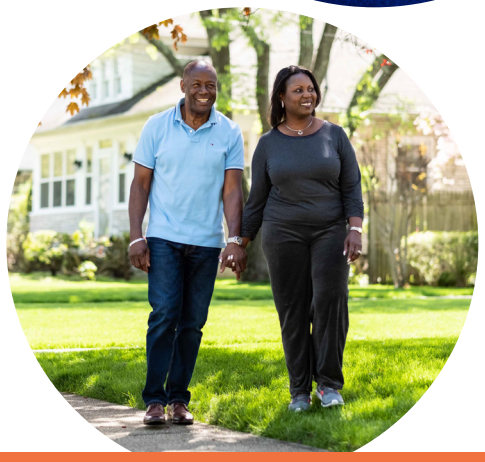
If your insurance denies payment, Exact Sciences will pursue appeals on your behalf where appropriate, and if appeal options are available. This process may take several months and you may receive a denial letter from your insurance company.[2]

You may receive multiple Explanation of Benefits (EOB) from your insurance. You will only receive a bill that looks like the one shown on the reverse, if payment is required after your claim is fully processed. Contact the GAP support team to discuss payment terms and financial assistance that may be available to you.[3]

If you are insured through government health coverage programs, Exact Sciences bills your insurance once testing is complete.

If your insurance denies payment, contact the GAP support team to determine what options might be available to you.[3]

If you don't have insurance, the GAP support team will help you determine your eligibility for financial assistance and explore the best options available to you.[3]



1. *If your insurance coverage was not in effect on the date of service, we will follow up with you for updated insurance information. If you do not have updated insurance, you will be billed for the cost of the test. You may be eligible for Financial Assistance and payment terms.*
2. *In some cases, consent to appeal is required. If your insurance company requires consent for Exact Sciences to appeal on your behalf, we will contact you. It is important to sign and return consent forms as soon as possible to allow timely aappeals in case the claim is denied.*
3. *Financial Assistance eligibility is based on Federal guidelines.*

Contact us to learn more about how GAP may be able to help you at: **1-888-662-6897, option 2**

oncoExTra™

oncotype DX® Breast DCIS Score

oncotype DX® Breast Recurrence Score

riskguard™ Hereditary Cancer Test

oncotype DX® Colon Recurrence Score

EXACT SCIENCES

Please note that Exact Sciences is currently unable to accept orders for the OncoExTra™ test for patients whose specimen was collected in or originated from the state of New York. We are working diligently to obtain the appropriate New York State Department of Health (NYSDOH) permit so that we are able to accept such orders in the future.

EXACT SCIENCES BILLING PROCESS

Step 1:
Your doctor orders the test.

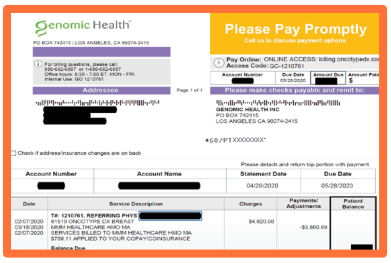
Step 2:
Exact Sciences bills your insurance once testing is complete and we confirm your insurance details.[1]

Step 3:
Insurance processes your claim. Please sign and return the enclosed consent form as soon as possible to allow timely appeals in case the claim is denied.[2]

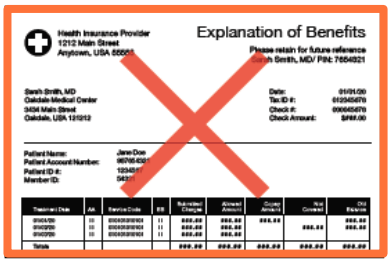
Step 4:
You should receive an Explanation of Benefits (EOB) from your insurance company. THIS IS NOT A BILL. Out of pocket costs for the test, if any, are determined by your insurance company.[3]

Step 5:
Where appropriate, and if appeal options are available, Exact Sciences will pursue appeals on your behalf. This may take several months and you may receive a denial letter from your insurance.

You may receive multiple EOBs from your insurance and will receive a bill that looks like the one below if payment is required after the claim is fully processed. Do not make a payment until then.



SAMPLE BILL



NOT A BILL

1. If your insurance coverage was not in effect on the date of service, we will follow up with you for updated insurance information. If you do not have updated insurance, you will be billed for the cost of the test. You may be eligible for Financial Assistance and payment terms.
2. Consent form allows Exact Sciences to appeal if the claim is denied. Please send to odxclaimsupport@genomichealth.com or mail to: PO Box 742415, Los Angeles, CA 90074-2415
3. Please call your insurance if you have specific questions regarding your insurance coverage.

About Exact Sciences

A leading provider of cancer screening and diagnostic tests, Exact Sciences helps people get the answers they need to make more informed decisions across the cancer continuum. Building on the success of the Cologuard®, Oncotype® and **OncoExTra™** tests, Exact Sciences is investing in its product pipeline to take on some of the deadliest cancers and improve patient care. Through an innovative, rigorous approach, and with the support of visionary collaborators, we're helping advance the fight against cancer.

EXACT SCIENCES