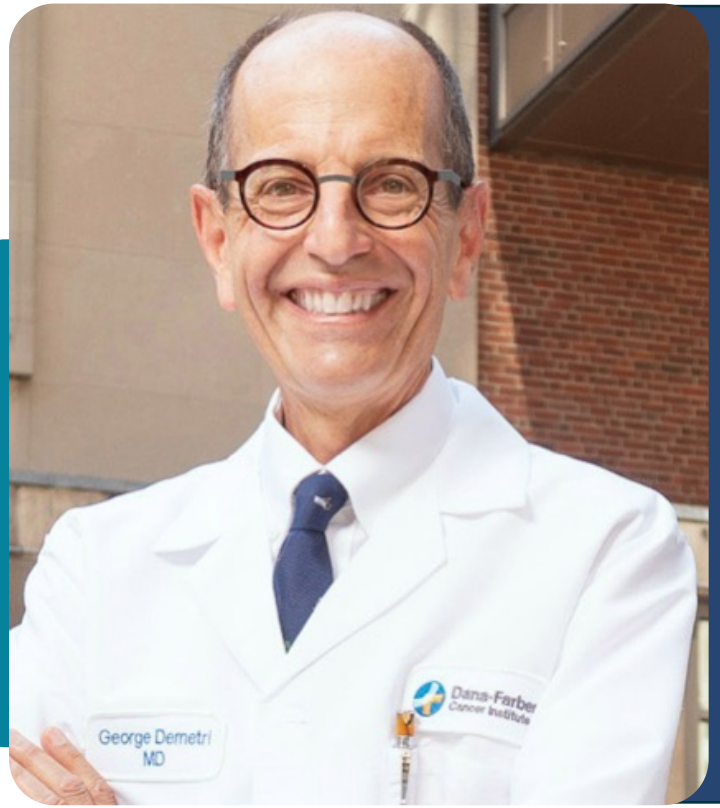
A Clinical Trial for Patients with Metastatic Cancer of Any Solid Tumor Type with an Inactivating *TSC1* or *TSC2* Genetic Mutation

An Educational Webinar

ADI bioscience



George Demetri, MD

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Dr. Demetri is a paid consultant to Aadi Bioscience.

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Willis Navarro, MD

Dr. Navarro is Vice President, Clinical Sciences and Pharmacovigilance at Aadi Bioscience.

The safety and efficacy of *nab*-sirolimus in *TSC1* and *TSC2* solid tumors have not been established.

Agenda

What is a Basket Trial/Pan-Tumor Study?

Why You Should Care About *TSC1* and TSC2

nab-sirolimus Mechanism of Action

How Your Members can Find Out if They Have a *TSC1* or *TSC2* Mutation

What is PRECISION 1 and How is it Different? (Just-in-Time Model)

How to Participate in PRECISION 1

The safety and efficacy of *nab*-sirolimus in *TSC1* and *TSC2* solid tumors have not been established.

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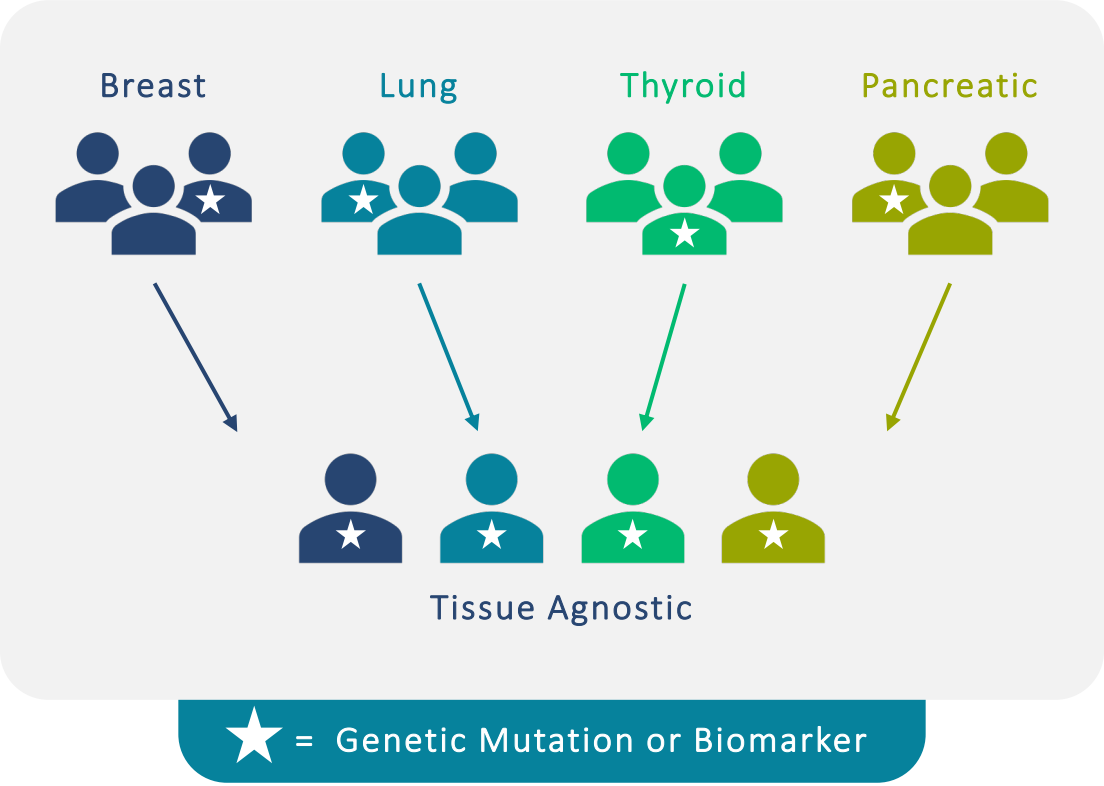
What is a **Basket Trial/ Pan-tumor** Study?

A Pan-Tumor (or Tissue-Agnostic) Clinical Trial Tests a Treatment Across **Multiple Tumor Types**



- In traditional clinical trials, treatments are usually tested in specific tumor types based on the tissue of origin, such as breast cancer, lung cancer, or colon cancer.
- However, in pan-tumor (or tumor-agnostic) clinical trials, the focus shifts from the tumor's tissue of origin to specific genetic mutation or biomarkers that are shared across different types of cancer.

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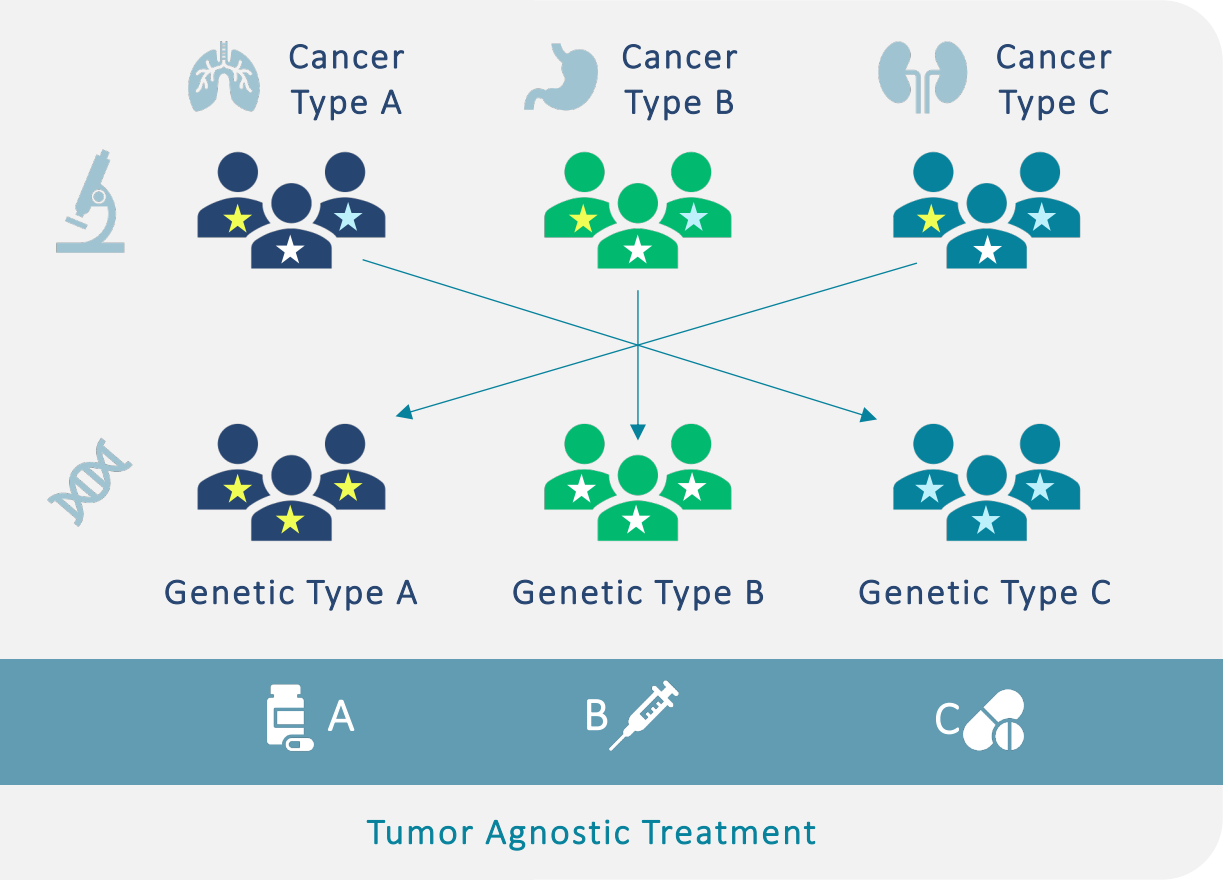
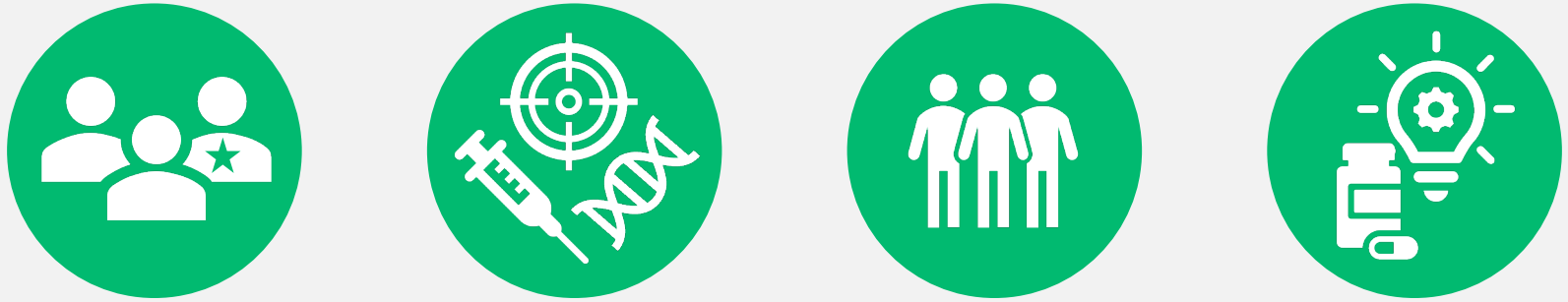
Pan-Tumor (or Tissue-Agnostic) Clinical Trials Can be Used For **Many Treatment Types**



- The primary objective of pan-tumor clinical trials is to identify and evaluate the effectiveness of therapies that target specific genetic mutations or biomarkers present in multiple tumor types.
- These genetic mutations or biomarkers may drive cancer growth and survival, making them attractive targets for treatments.

What Makes a **Pan-Tumor Trial so Powerful?**



Biomarker or Mutation-Driven Selection

Precision Medicine

Inclusivity

Potential for **Faster Drug Development**

Overall, pan-tumor clinical trials represent a promising approach in advancing cancer research and treatment by identifying therapies that can benefit patients with different types of cancer carrying specific genetic mutations or biomarkers.

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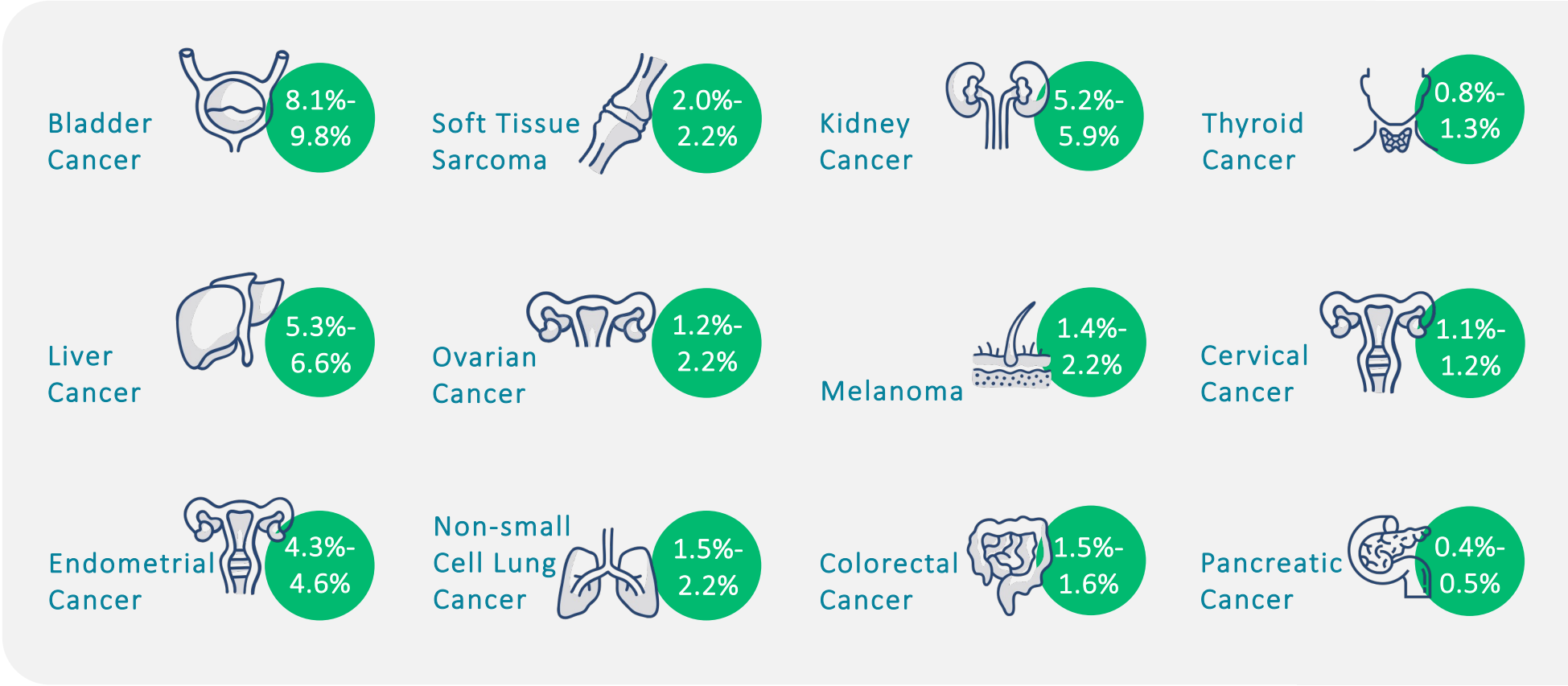
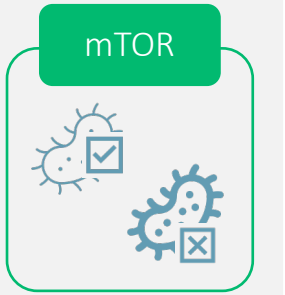
Why Should You Care About *TSC1* and *TSC2*?

TSC1 and *TSC2* Mutations Can Occur in **Many Common Cancer Types**

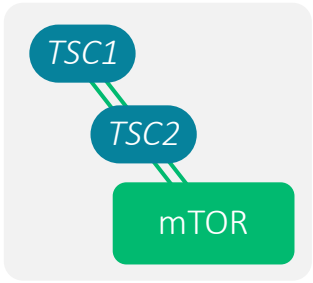
Changes, called **mutations**, in *TSC1* and *TSC2* may occur in different types of cancers, including:



Targeted Therapy Approaches for **mTOR-Driven Cancers**

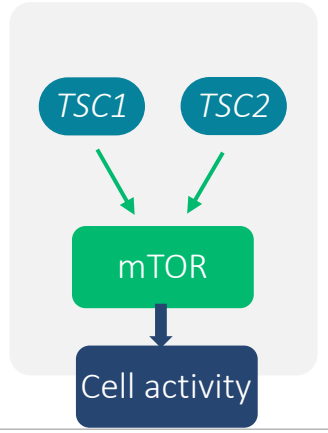


mTOR is a protein that helps to control the growth and functions of both normal and cancer cells.

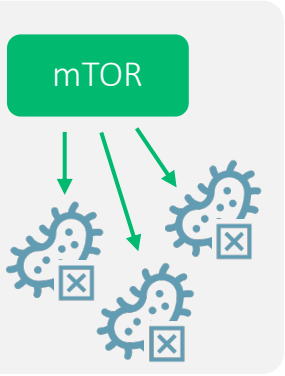


The *TSC1* and *TSC2* genes are part of the mTOR pathway.

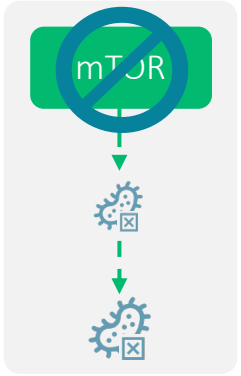
*A pathway is a series of actions within a cell that lead to a certain product or changes.



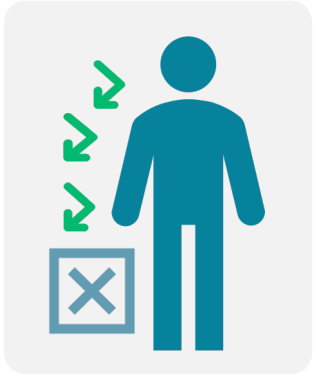
The genes in the mTOR pathway work together to CONTROL the mTOR pathway.



Loss of *TSC1* or *TSC2* leads to overactive mTOR, resulting in uncontrolled growth of cancer calls.



By inhibiting mTOR, mTOR-targeted therapies can help to slow down the mTOR pathway, potentially slowing the growth of a tumor.



One problem with oral mTOR-targeted therapies is that they are not easily absorbed by the body, which limits their effectiveness.

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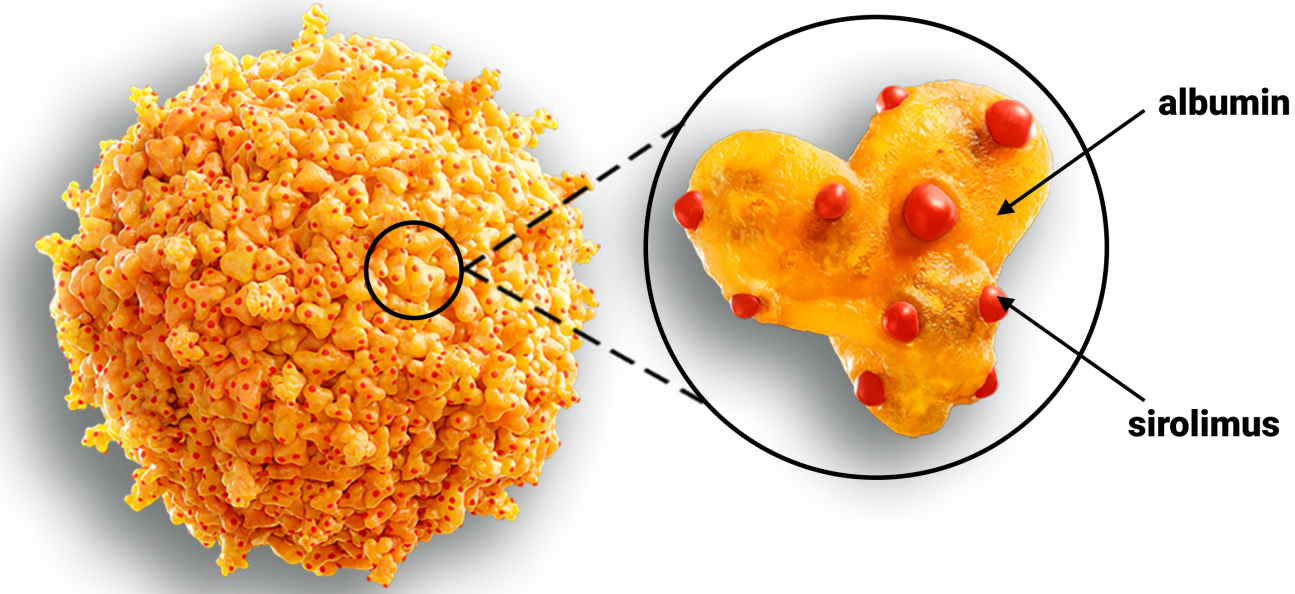
nab-Sirolimus: An **Investigational Targeted Therapy** for Tumors with *TSC1* or *TSC2* Mutations



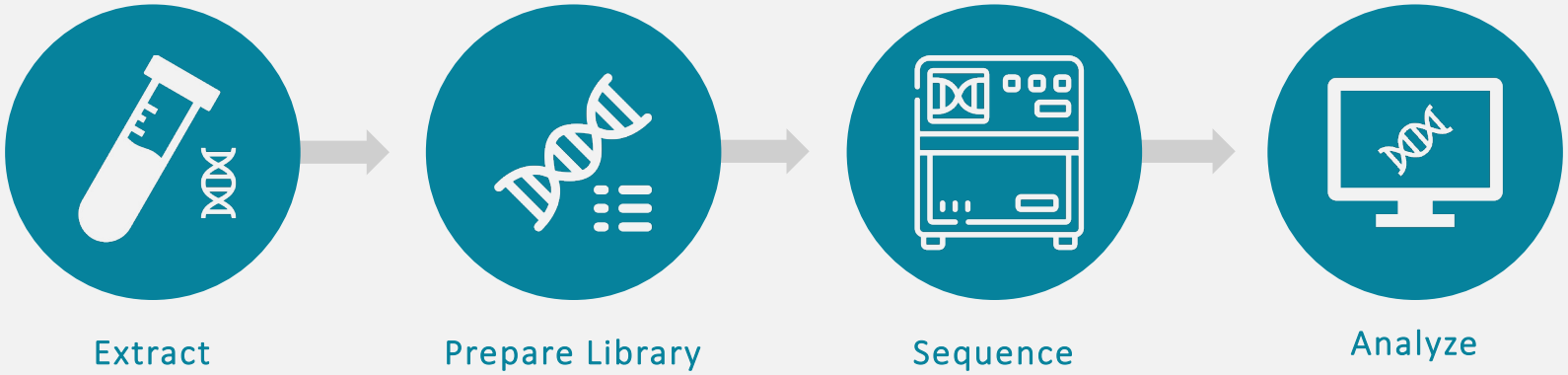
- *nab* technology binds sirolimus to albumin, a protein that is actively absorbed by tumors.
- Pre-clinical studies have shown that *nab* technology potentially delivers more sirolimus to the tumor than an oral formulation of the drug.
- In nonclinical studies, *nab*-sirolimus slowed tumor growth.
- *nab*-sirolimus is administered by IV-infusion.

The safety and efficacy of *nab*-sirolimus in tumors with *TSC1* or *TSC2* mutations have not been established.

How **Patients** Can Find Out if They Have a *TSC1* or *TSC2* Mutation

Next-Generation Sequencing

A **New Dimension** of **Diagnostics** to Help Choose **Treatment**



- Next-generation sequencing (NGS) is a powerful technology that involves analyzing the genetic material (DNA and RNA) of a patient's tumor to identify specific genetic alterations.
- *TSC1* and *TSC2* genes are included for testing in most standard commercial NGS tests.

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Current NGS Tests Identify Pathogenic Inactivating *TSC1* and *TSC2* Alterations

Company	Test Name	*TSC1* and *TSC2*	*# Genes Analyzed*
Ambry Genetics®[1]	CancerNext-*Expanded*®	✓	*77*
	RenalNext®	✓	*20*
	TSC1/TSC2 seq and del/dup	✓	*2*
Caris® Life Sciences[2]	MI Tumor Seek™	✓	*~22,000*
Foundation Medicine[3]	FoundationOne® CDx	✓	*324*
	FoundationOne® Liquid CDx	✓	*311*
GeneDx[4]	Comprehensive Common Cancer Panel	✓	*49*
	Renal Tumor Panels	✓	*18*
Guardant[5]	Guardant360® CDx	*TSC1*	*55*
Myriad[6]	Precise™ Tumor	✓	*523*
Resolution Bioscience[7,a]	Agilent Resolution ctDx FIRST	✓	*109*
Tempus[8]	Tempus xT	✓	*648*
	Tempus xF	✓	*105*

Some academic institutions have their own assays for evaluating many of the same genes analyzed in commercial tests[9,10]

[a] A part of Agilent.

DEL, deletions; INDEL, insertion-deletion mutation; SNV, single-nucleotide variant; *TSC1*/*TSC2*, tuberous sclerosis complex subunit 1/2.

1. Ambry Genetics. Accessed January 30, 2023. https://www.ambrygen.com/providers/oncology/test-menu#test-by-gene **2.** Caris Molecular Intelligence. Accessed January 30, 2023. https://www.carislifesciences.com/wp-content/uploads/2020/08/MI-Tumor-Seek-Profile-Menu.pdf **3.** Foundation Medicine®. Accessed January 30, 2023. https://www.foundationmedicine.com/portfolio **4**. GeneDx. Accessed January 30, 2023. https://www.genedx.com/tests/oncology~c9675 **5.** Guardant Health. Accessed February 3, 2023. https://guardanthealth.com/products/tests-for-patients-with-advanced-cancer/ **6.** Myriad. Accessed January 30, 2023. https://myriad.com/genetic-tests/precise-tumor/ **7.** Resolution Bioscience. Accessed February 3, 2023. https://www.resolutionbio.com/assays/Resolution-ctDx-FIRST.html **8.**Tempus. Accessed February 3, 2023. https://www.tempus.com/oncology/geno **9**. Memorial Sloan Kettering Cancer Center. Accessed January 30, 2023. https://www.mskcc.org/msk-impact **10.** UW OncoPlex Cancer Gene Panel. Accessed January 30, 2023. https://testguide.labmed.uw.edu/view/OPX

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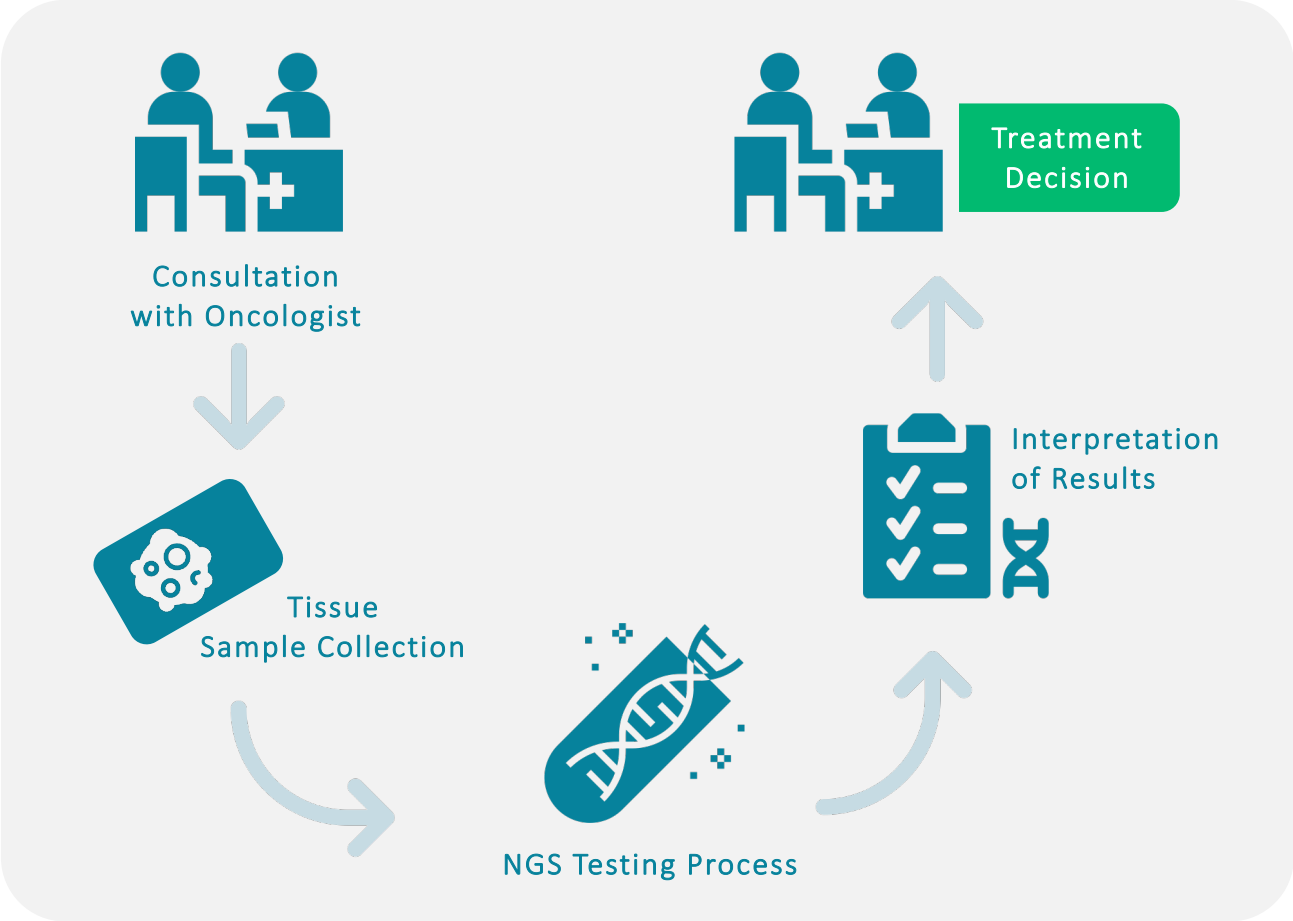
How Patients Get **Next-Generation Sequencing** for Their Cancer



While NGS can provide valuable information, it may not be suitable for every patient.
The decision to undergo NGS testing should be made in consultation with the patient's healthcare team, taking into account the specific characteristics of the cancer, other options for testing, and the patient's overall health and preferences. Also ask about the potential to use NGS testing on a blood sample rather than tumor. Finally, ask about the cost of testing.

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What is PRECISION 1?

Precision 1: **Study Schema**

Key Eligibility Criteria

To be eligible for the trial, a patient must:

- Be at least 12 years old
- Not have used any other mTOR inhibitors (for example, never had any everolimus or temsirolimus)
- Be able to perform normal daily activities (measured by a doctor using certain scales)
- Have a cancer with a specific type of *TSC1* or *TSC2* mutation that cannot be cured by any standard means

Treatment and Follow-up

Arm A: Patients with specific *TSC1* mutations (n=~60)

Arm B: Patients with specific *TSC2* mutations (n=~60)

- *nab*-sirolimus administered as an intravenous infusion over 30 minutes

nab-sirolimus Dosing Schedule

Repeat until disease progression, unacceptable toxicity, withdrawal of consent, or at investigator discretion

Primary Endpoint: Objective Response (ORR): The percentage of people in a study or treatment group who have a partial response or complete response to the treatment within a certain period of time. A partial response is a decrease in the size of a tumor or in the amount of cancer in the body, and a complete response is the disappearance of all signs of cancer in the body. ORR was determined by independent radiology review (RECIST v1.1)

nab-sirolimus is Investigational in this setting; safety and efficacy have not been established for this use.

How is **PRECISION 1** Different?

The “Just-in-Time” Model

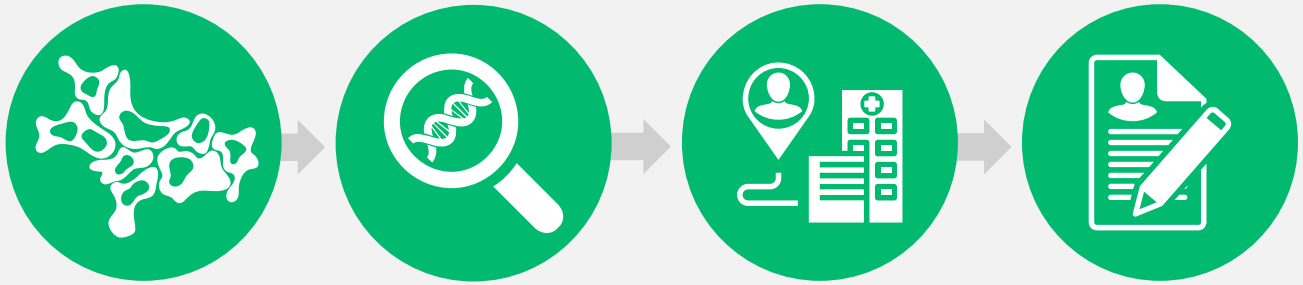
Expanding PRECISION 1 Access to Patients

Enabling Trial Participation **Where the Patients Are**

Aadi is enabling eligible patients to participate in the trial from wherever they are comfortable receiving care.

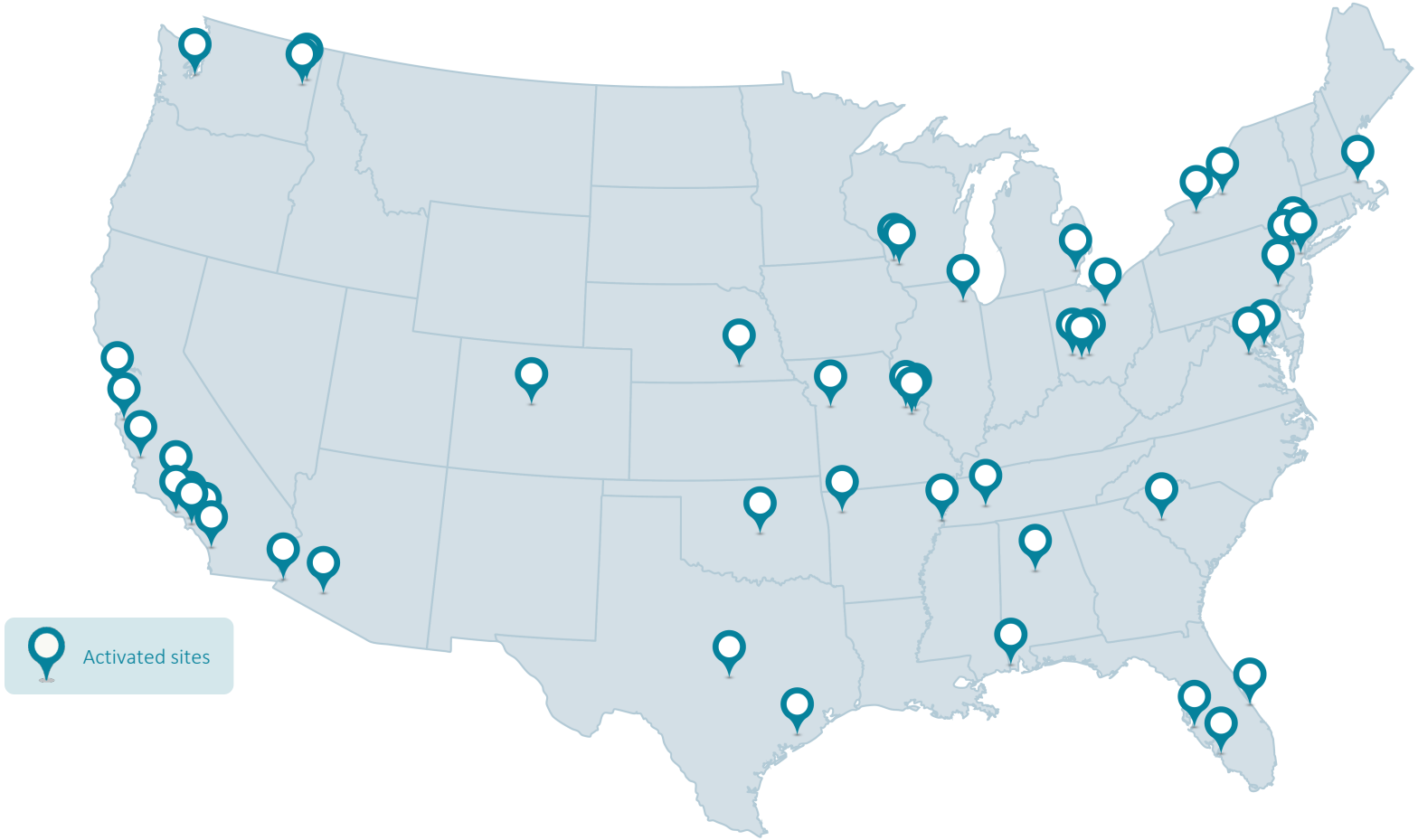
No need to travel to a separate trial site.

When a patient is identified, the patient and their doctor choose where trial-related care will take place; the “just-in-time” model.



PRECISION 1 Sites Span **Key Regions** and **Leverage Unique Partnerships**[1,2]

PRECISION 1 Trial Sites and Just-in-Time / Right-in-Time Sites[1,2]



For information about trial sites, please visit ClinicalTrials.gov.

For more information about the trial, please contact Aadi Medical Information at 888-246-2234.

PRECISION1

1. Clinicaltrials.gov. NCT05103358. Accessed August 8, 2022. https://clinicaltrials.gov/ct2/show/NCT05103358

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How to **Participate** in PRECISION 1

For More Information:
Talk to your doctor and visit **Precision1TrialInfo.com**

You or your doctor can contact Aadi Bioscience Medical Information at 1-888-BIO-AADI (888-246-2234) or medinfo@aadibio.com

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