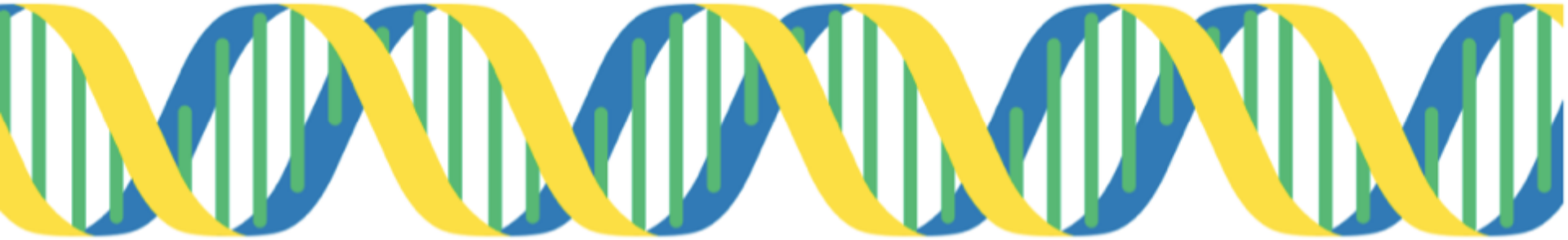
Partnering directly with patients to accelerate translational cancer research

Nikhil Wagle

Genomic Medicine 10

May 2017



BROAD INSTITUTE

DANA-FARBER CANCER INSTITUTE

A Paradigm Shift: The Genomic View of Cancer

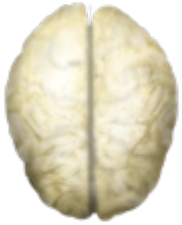
From Anatomy…

Lung

Breast

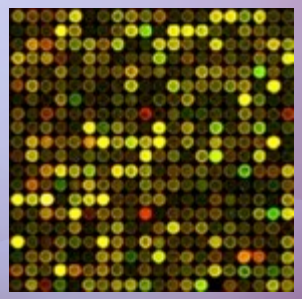
Prostate

Colon

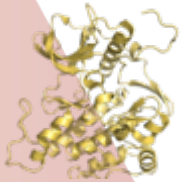


Brain

GENOMIC/MOLECULAR PROFILING

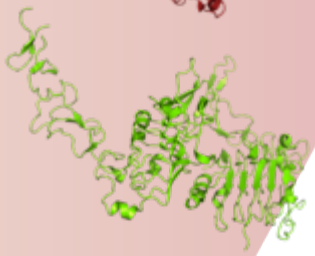


To Genetic Mutation



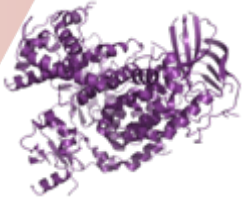
KIT (Imatinib)

EGFR (Erlotinib)



HER2 (Trastuzumab)

BRAF (Vemurafenib)



PIK3CA (BYL719)

A Paradigm Shift: The Genomic View of Cancer

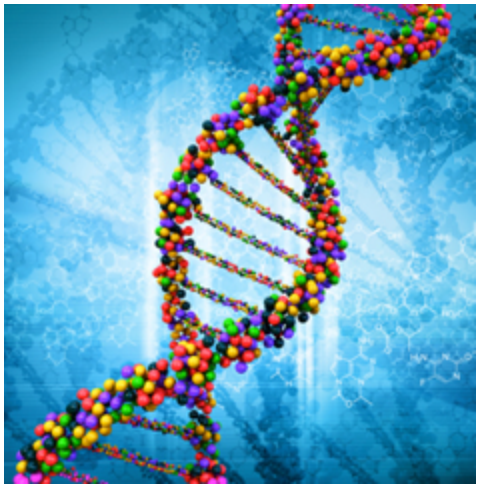
vemurafenib

Pre-treatment

15wks on vemurafenib

Wagle, Emery *et al*, *Journal of Clinical Oncology*, 2011

Accelerating Cancer Precision Medicine

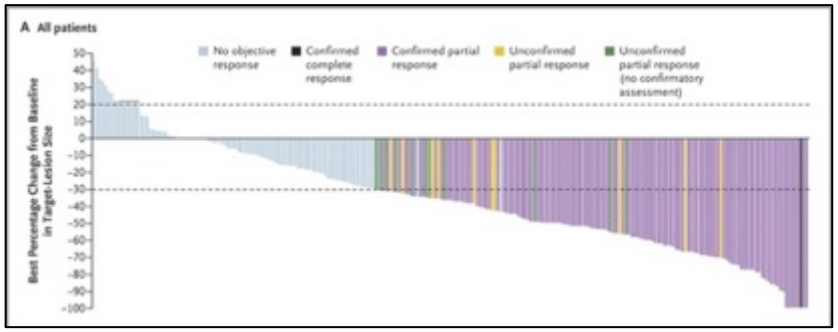


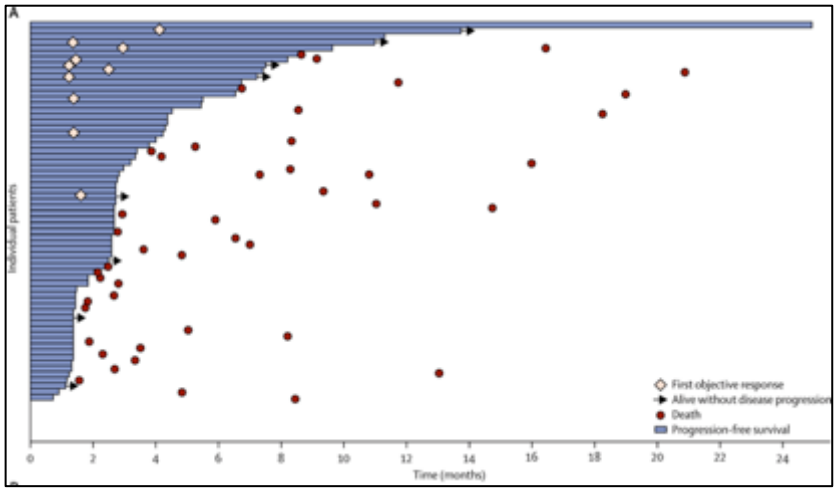
- **Ultimate goal:** To understand what drives cancer so that we eventually can interpret every patient's cancer genome, identify the optimal treatments, and anticipate and preempt resistance before it arises

- There's been a lot of progress, but we have more work to do

- What will it take to get there? Detailed molecular and genomic characterization of thousands of tumor and germline samples along with medical information

Why Study Extraordinary Responses?



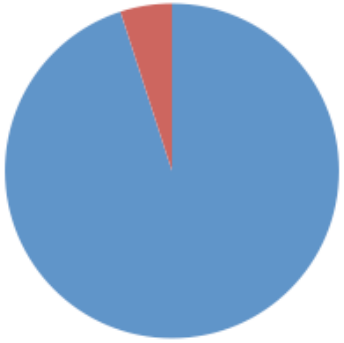


Enormous diversity in response of patients to anti-cancer drugs - and we do not understand why

- Many agents in clinical trials "fail" and are abandoned – even though they have profound activity in a few patients
- Large numbers of patients being treated with drugs to which they will develop toxicity but derive no benefit

Studies of extraordinary responders could help develop methods for optimally matching patients to drugs, highlight effective uses for "failed" therapies, and aid with development of new therapies

Challenges of Studying Patient Tumor Samples



Only 5% of U.S. cancer patients are enrolled in clinical trials

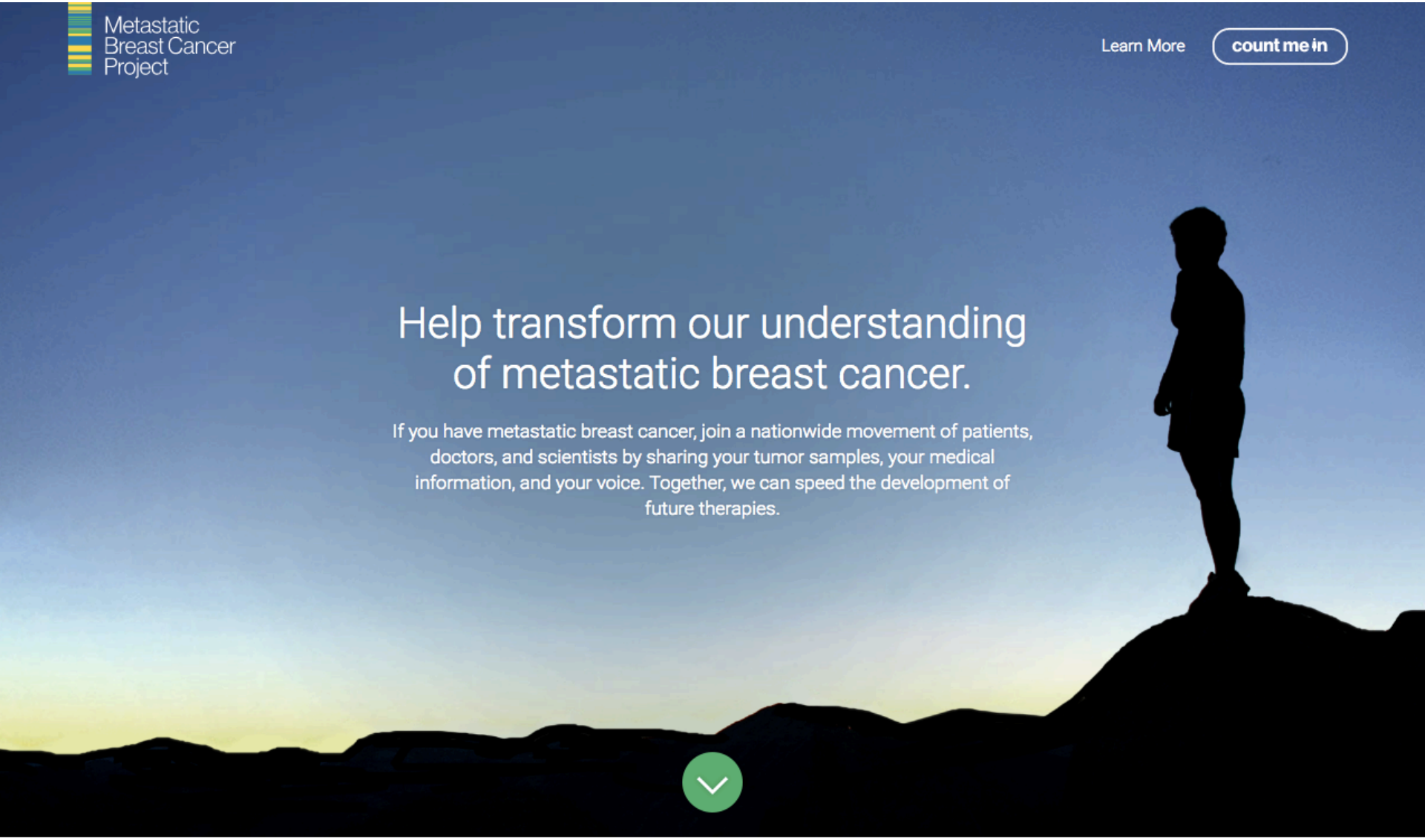
85% of U.S. cancer patients are treated in community settings

Most tumor samples have not been readily available for study

Technology, social media, and cultural changes now provide a new opportunity to engage cancer patients and directly partner with them in this research

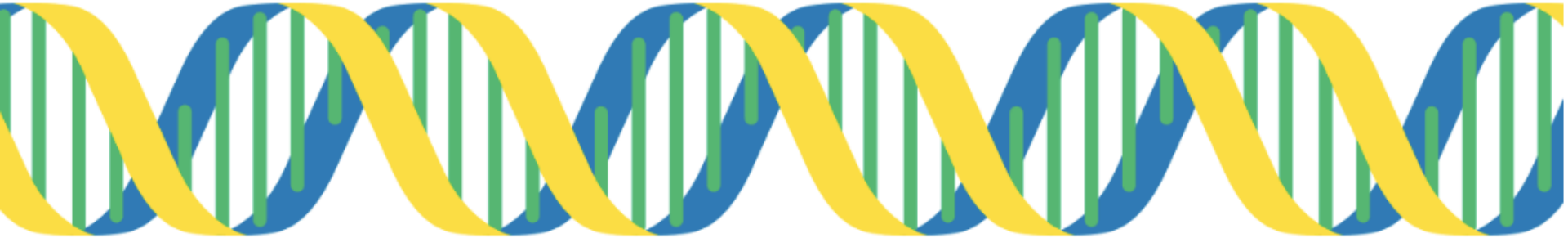
The Metastatic Breast Cancer Project

MBCproject.org



Your tumor and medical records could unlock discoveries.

The unique genetic information in your cancer could hold the key to rapid advances in cancer treatment. By looking at the DNA in your samples (using "genomic sequencing"), researchers can make discoveries to identify new ways to treat metastatic breast cancer. This information will be securely shared with researchers around the world. It will be invaluable to cancer research for years to come — and ultimately lead to a better understanding and faster advances in the treatment of metastatic breast cancer.



BROAD INSTITUTE

HARVARD MEDICAL SCHOOL

DANA-FARBER CANCER INSTITUTE

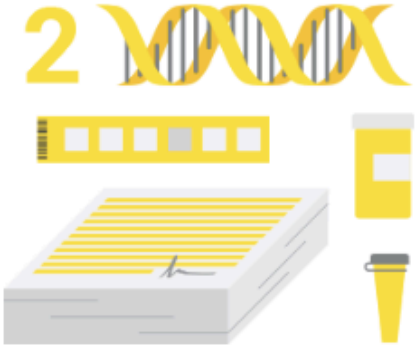
Become part of the research movement. Have a direct impact on the future.

By saying "Count Me In", you will partner with leading research institutes, hospitals, and patient advocacy groups by sharing part of your stored tumor tissue and copies of your medical records.

Here's how you can participate

Step 1. Tell us about yourself

Click "Count Me In" and complete a simple online form to tell us about yourself and your cancer. Our goal is to perform many different studies within the metastatic breast cancer community, so allowing us to know a little bit about your experience will help us design future



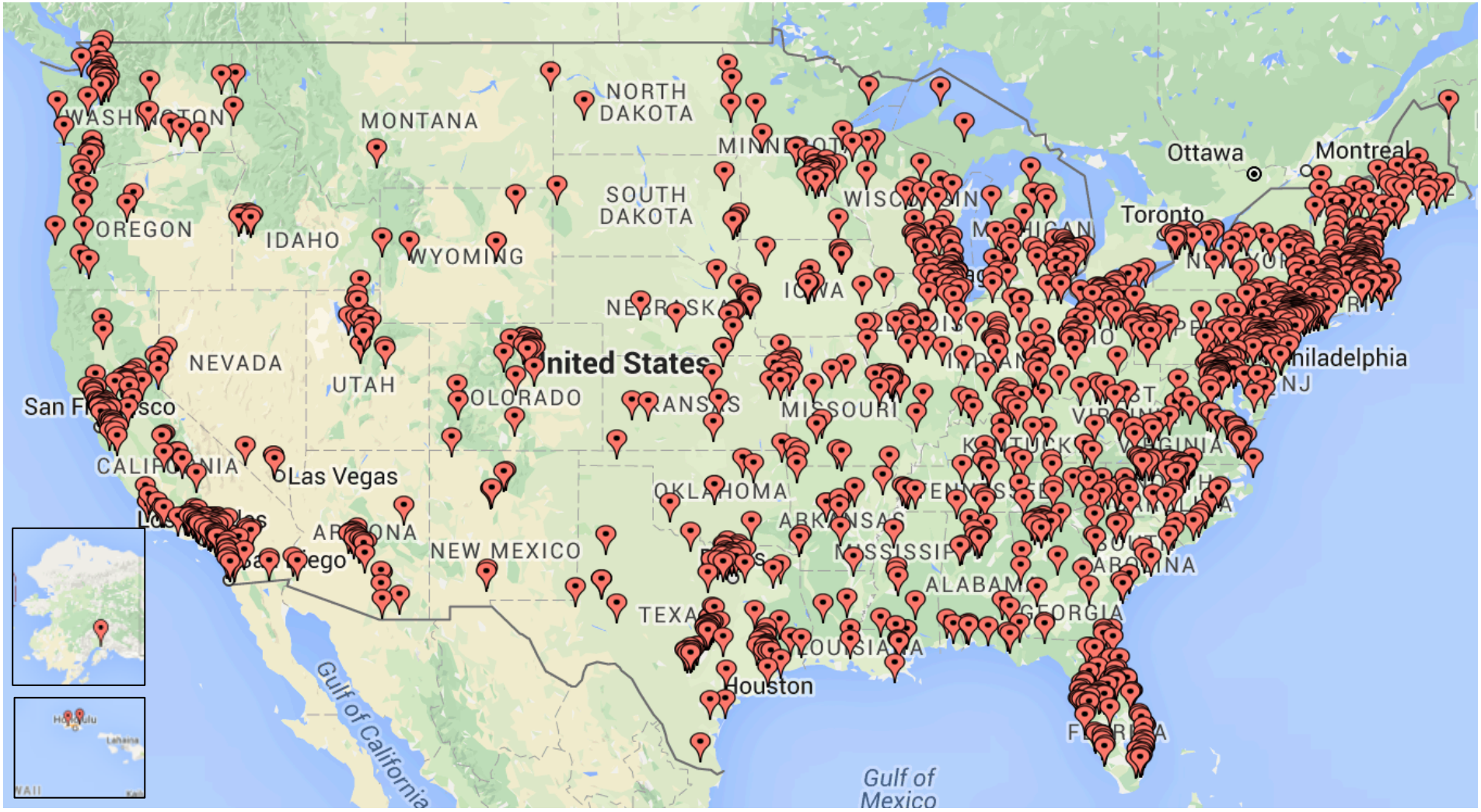
Step 2. Give us permission to collect your samples and data

When we start a study that matches what you have told us about yourself, we will ask you to fill out an online consent form that requests your permission to obtain copies of your medical records and some of your stored tumor tissue. We will do the rest - we'll contact

Step 3. Learn with us along the way

We are excited to learn with you! Throughout the project, we will provide you with regular updates about the status of the project and share any discoveries that you have enabled us to make. We also may ask you additional questions about your experience to help with

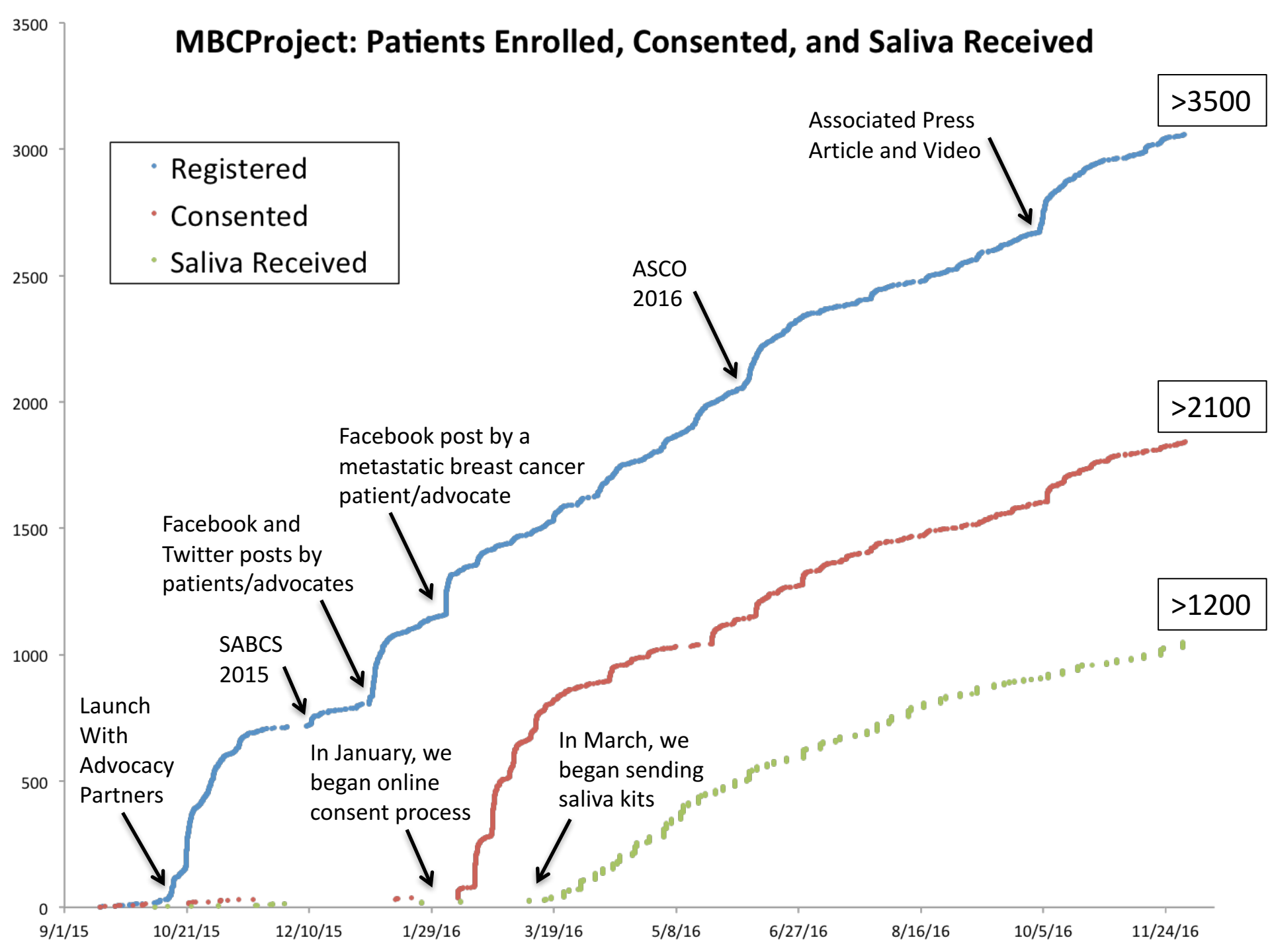
The Metastatic Breast Cancer Project
MBCproject.org



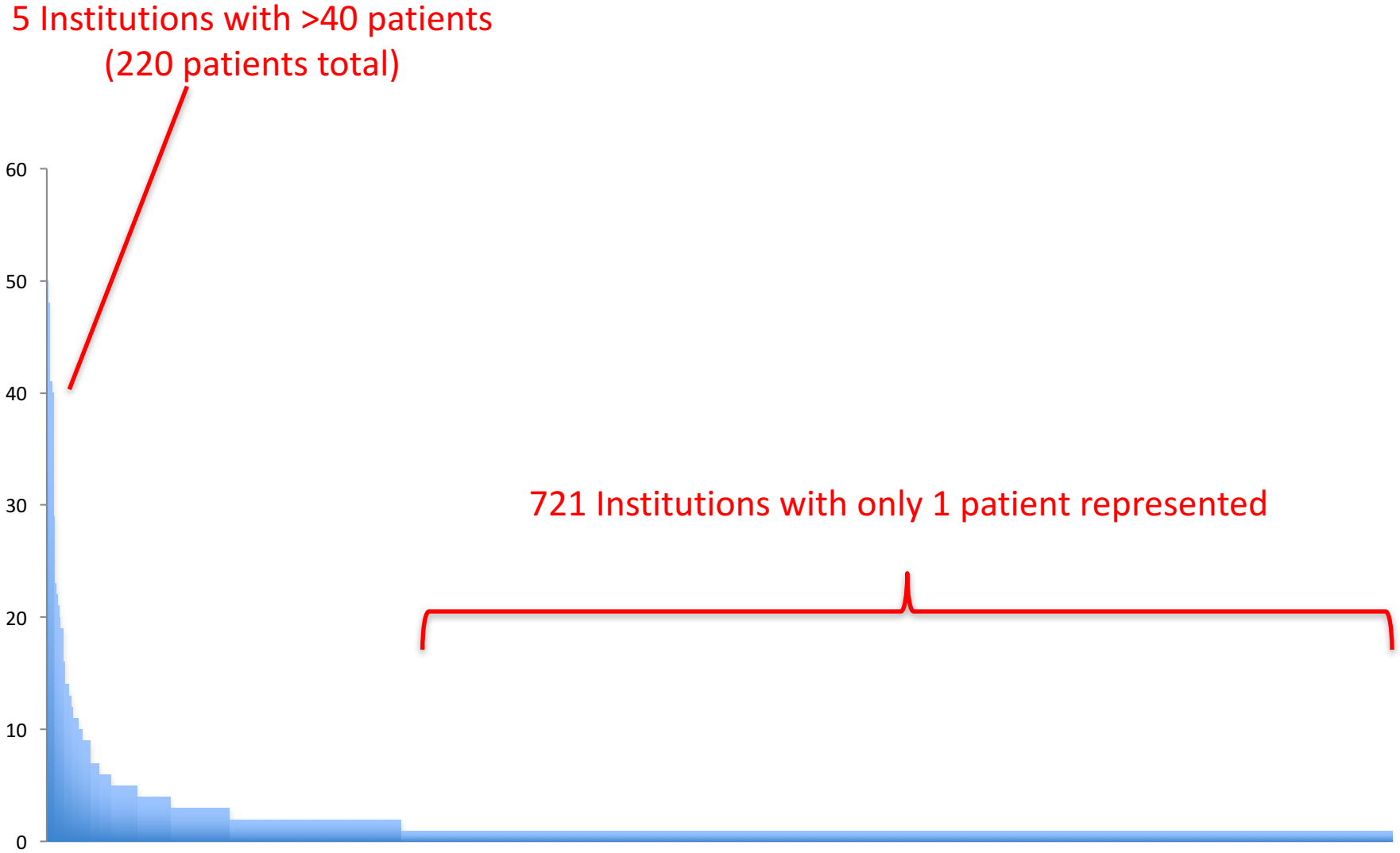
*Over **<u>3500 women and men</u>** with metastatic breast cancer from all 50 states have joined the MBCproject since our launch in October 2015*

Metastatic Breast Cancer Project: Approach

1. ONLINE CONSENT	*Electronic consent form asks patients for permission to obtain a saliva sample, tumor tissue and medical records.*
2. SALIVA COLLECTION	*Consenting patients are sent a saliva kit and asked to mail back their saliva sample*
3. MEDICAL HISTORY	*Medical records are obtained by the MBCproject team and centrally reviewed and abstracted*
4. TISSUE COLLECTION	*Tumor blocks requested from local pathology departments by the MBCproject team*
5. GENOMIC ANALYSIS	*Molecular characterization of tumor and saliva includes whole exome sequencing (WES) and transcriptome sequencing (RNASeq)*
6. INTERPRETATION	*Genomic data is interpreted in the context of clinical data (extraordinary response, de novo disease, age, etc) at the individual level and in aggregate across similar patients*
7. REPORTING / DATA SHARING	*De-identified genomic & clinical data shared widely with research community. Overall progress, findings, and discoveries regularly communicated directly to patients*


MBCProject: Patients Enrolled, Consented, and Saliva Received
Registered
Consented
Saliva Received
>3500
>2100
>1200
Associated Press Article and Video
ASCO 2016
Facebook post by a metastatic breast cancer patient/advocate
Facebook and Twitter posts by patients/advocates
SABCS 2015
Launch With Advocacy Partners
In January, we began online consent process
In March, we began sending saliva kits
3500
3000
2500
2000
1500
1000
500
0
9/1/15
10/21/15
12/10/15
1/29/16
3/19/16
5/8/16
6/27/16
8/16/16
10/5/16
11/24/16

992 Institutions Represented Among 2000 Consented Patients



Patient-Reported Data

95% submitted the 16-question survey

98% response rate to each question (all are optional)

6 minutes to complete

Detailed patient reported data from >3300 patients

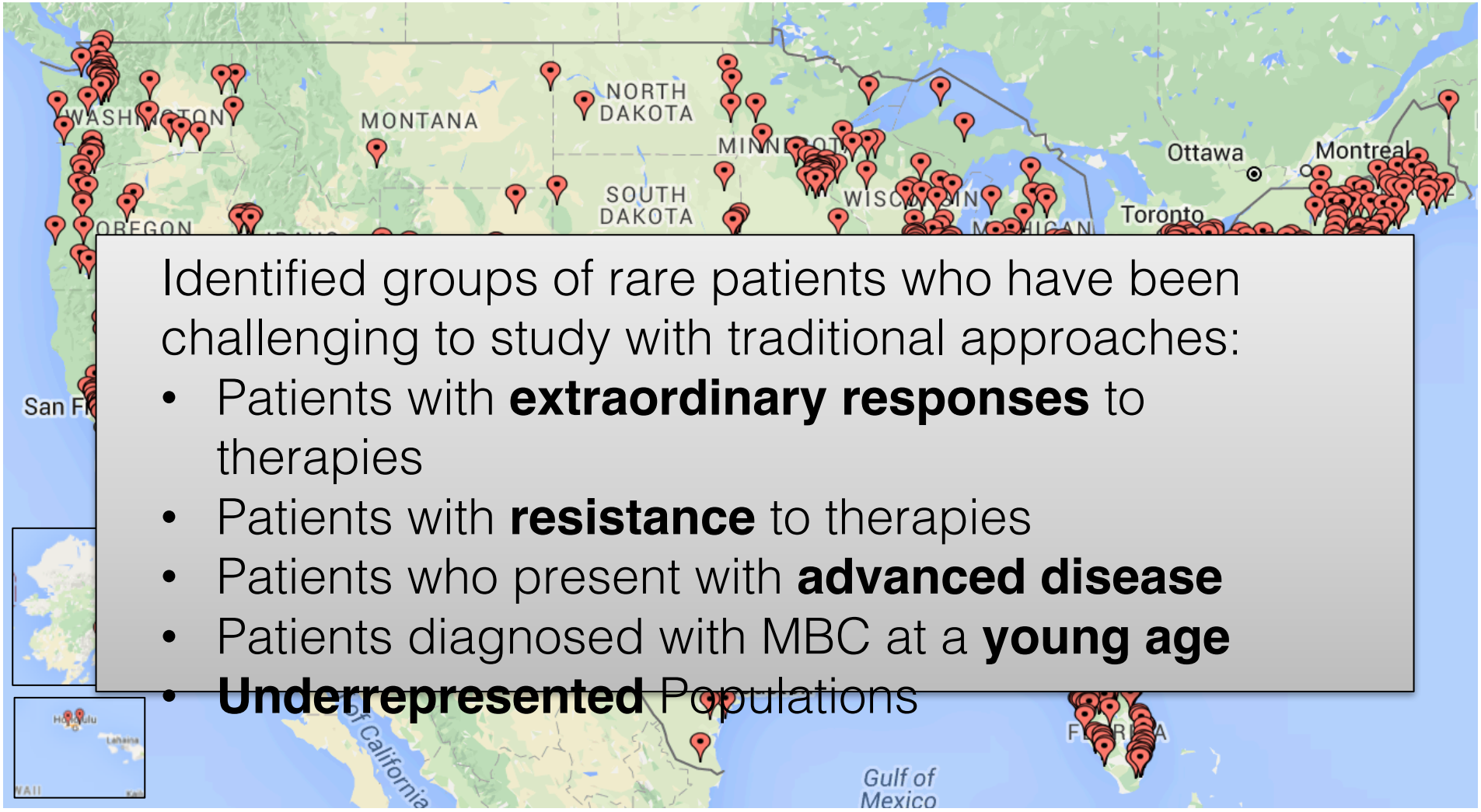
Disease Characteristics:
- *Dates of initial diagnosis*
- *Date of diagnosis with metastatic disease*
- *ER+, PR+, and HER2+ status*

Treatment Response:
- *Questions about extraordinary responses*
- ***Free text** about treatments*
- *Date of most recent biopsy*

Demographics:
- *Year of birth*
- *Race and ethnicity*

***Free text** about anything additional*

The Metastatic Breast Cancer Project
MBCproject.org

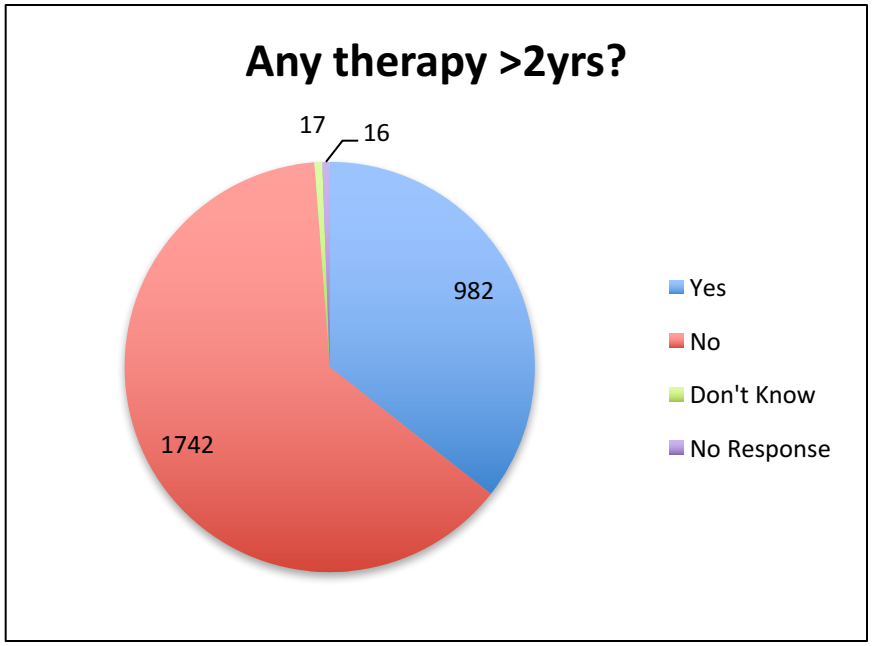


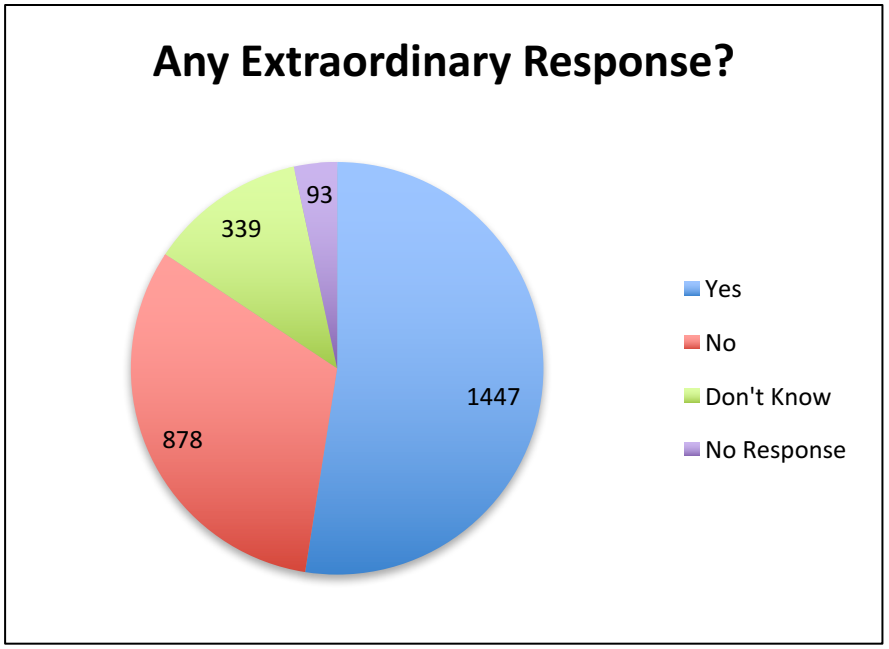
Identified groups of rare patients who have been challenging to study with traditional approaches:

- Patients with **extraordinary responses** to therapies
- Patients with **resistance** to therapies
- Patients who present with **advanced disease**
- Patients diagnosed with MBC at a **young age**
- **Underrepresented** Populations

*Over **3400 women and men** with metastatic breast cancer from all 50 states have joined the MBCproject since our launch in October 2015*

Studying patients with Exceptional Responses





99% of those who responded "Yes" provided the drug names

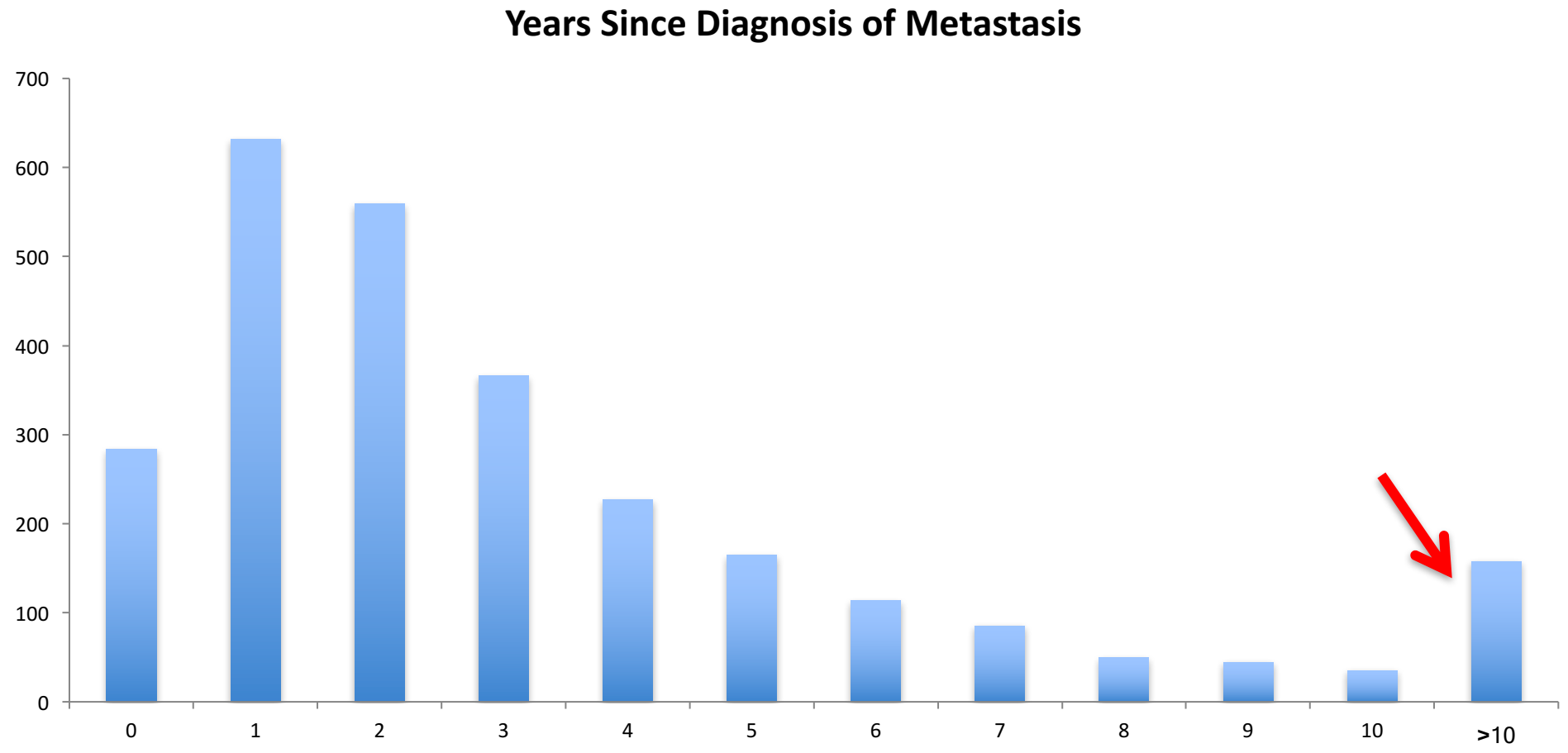
98% of those who responded "Yes" provided drug names and additional "free text" details

***Hundreds of** patients with self-reported long-term and/or exceptional responses identified. For example:*

- ***Capecitabine (Xeloda)**: 138*
- ***Platinums (Carboplatin, Cisplatin) and PARP inhibitors:** 101*
- ***Everolimus**: 41*
- ***Palbociclib: 127***

Studying patients with Exceptional Responses

158 respondents report living with metastatic disease for more than 10 years.



As of October 2016, Based on 2722 responses (98.7% response rate)

A Shared Clinico-genomic Database

NATIONAL CANCER INSTITUTE
GENOMIC DATA COMMONS

All somatic and germline genomic data and linked clinical data deposited every 6 months

Deposition from first 100-200 samples expected 1st half 2017

Metastatic Breast Cancer Project: PROJECTS

1) **Specific Patient Cohorts** (all patients, specific characteristics, received particular rx, racial/ancestral differences

2) **Outliers** (exceptional responders, young people, men with breast cancer, rare subtypes)

3) **Epidemiology** (risk factors, natural history of disease, time to relapse, pattern of metastases)

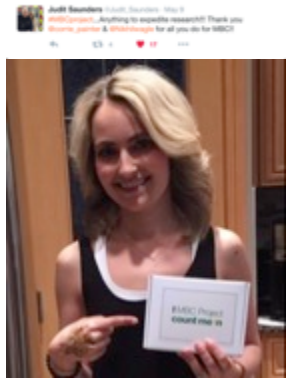
1) **Clinical Behavior** (response and resistance, side effects / toxicities)

2) **Real world practice patterns** (order of therapies, what are people getting in the community)

A Collaboration with Patients and Advocates

Patients and advocates have been involved from the beginning in conceiving, designing, implementing, testing, and refining this project.

“Count Me In”



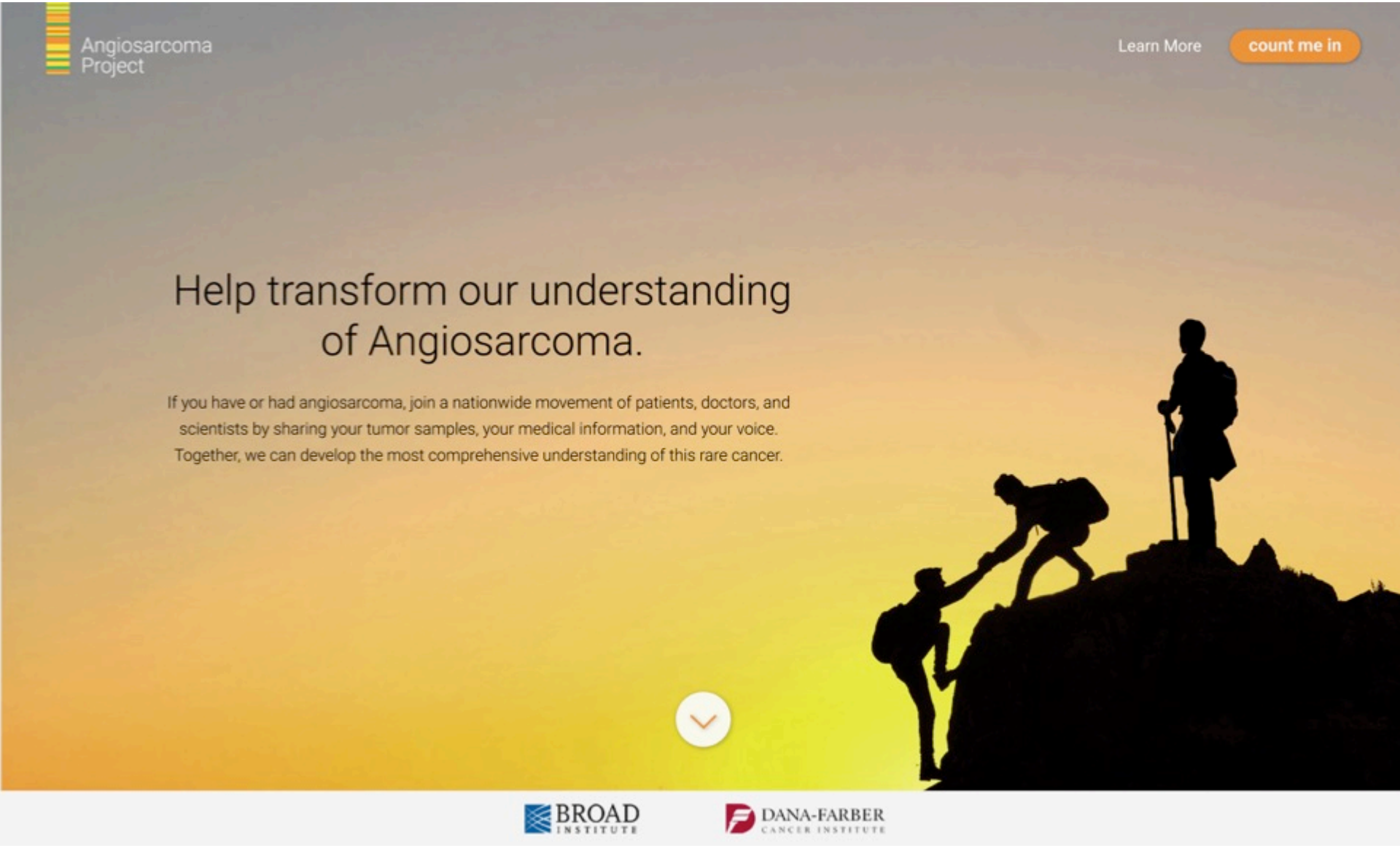
“I want to live and watch my children grow up, but if I can’t, then I want to leave a legacy and a cure.”
—Houston, TX

“As someone who does not live near a research center and therefore cannot easily participate in trials, I finally feel like I can contribute.”
—Lake Tahoe, CA

“Amazing how happy that little box makes you feel! I felt like a 2 year old. Let me help! I feel a sense of pride and belonging because of this.”
—Minneapolis, MN

“Giving us HOPE for the future and if not for some of us, for our families.”
—Scottsdale, AZ

The Angiosarcoma Project



The Prostate Cancer Project

Summary

- Partnering directly with patients through social media and patient/advocate partnerships enables *rapid* identification of large numbers of patients willing to share tumors, saliva, and medical records to accelerate research
- Enables study of rare patients (e.g. exceptional responders), otherwise challenging to find with traditional approaches
- A shared resource: all clinical and genomic data generated in this study will be shared widely with researchers
- Proof-of-concept study may serve as model for patient-driven research in other cancer types

Acknowledgements

- **Corrie Painter**
- **Elana Anastasio**
- **Michael Dunphy**
- **Mary McGuilllicuddy**
- **Jamie Holloway**
- Dewey Kim
- Jorge Buendia
- Esha Jain
- Erik Knelson
- Seth Wander
- Max Krevalin
- Sara Semonian
- Miguel Ilzarbe
- Eli Van Allen
- Kristen Zarrelli
- Tania Simoncelli
- Jesse Boehm
- Deb Dillon
- Jon Bistline
- Jared Cosulich
- Playground
- Carol Lowenstein
- Kristen Anderka
- Samira Bahl
- Alicia Wong
- Katie Larkin
- Sam Pollock
- Niall Lennon
- Sheila Fisher
- Stacey Gabriel
- Victor Adalsteinsson
- Gavin Ha
- Sam Freeman
- Greg Gyudish
- Sarah Reed
- Levi Garraway
- Nelly Oliver
- Karla Helvie
- Kate Mulherin
- Bina Venkataraman
- Bang Wong
- Mary Carmichael
- David Siedzik
- Scott Sutherland
- Lee McGuire
- Scott Sassone
- Lisa Girard
- Emily Lipscomb
- Andrea Saltzman
- Stacey Donneley
- Jenny Rood
- Jenn Chen
- Justine Levin-Allerhand
- Elizbeth Frank
- DFCI Advocates
- Eric Winer
- Eric Lander
- Todd Golub

Acknowledgements

*The **<u>many advocates and patients</u>** who have worked with us over the past year to develop and implement this project*

***<u>All of the patients with metastatic breast cancer</u>** who are participating and have contributed their voice to this project*

SUSAN F. SMITH
CENTER FOR
WOMEN'S CANCERS

DFCI / BWH / Broad
Center for Cancer Precision Medicine

DANA-FARBER
CANCER INSTITUTE

BROAD
INSTITUTE

DANA-FARBER/BRIGHAM AND WOMEN'S
CANCER CENTER

HARVARD MEDICAL SCHOOL

Thank you!

mbcproject.org

Questions? Email *info@mbcproject.org*

nikhil_wagle@dfci.harvard.edu
@nikhilwagle