SWOG
Leading cancer research. Together.

FNIH
Foundation for the National Institutes of Health

NCI
National Clinical Trials Network

DEPARTMENT OF HEALTH & HUMAN SERVICES • USA

FRIENDS of CANCER RESEARCH

Celebrating 4 Years of Lung-MAP

Where We've Been & Where We're Going

SWOG FALL MEETING
OCTOBER 5, 2018

LUNG-MAP

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Lung-MAP study leadership

- Vali Papadimitrakopoulou, MD – study chair
- Roy Herbst, MD PhD –study co-chair
- David Gandara, MD – study co-chair
- Mary Redman, PhD – lead statistician
- Phil Mack, PhD – TM co-chair
- Fred Hirsch, MD PhD – TM co-chair
- Karen Kelly, MD – lung committee chair
- Katie Minichiello, MS – study statistician
- Jieling Miao, MS – study statistician
- James Moon, MS – study statistician
- Louise Highleyman – lead study data coordinator
- Sarah Basse – SDMC project manager
- Dani Weatherbee – SDMC Applications Development
- Joni Harris – study data coordinator
- Leah Everheart – study data coordinator
- Crystal Miwa – Lead SWOG operations project managaer
- Mariah Norman – Study Protocol Coordinator/Project manager

Where We've Been

The Story of Lung-MAP

October 2011 – Creativity Inspiration motivated by TCGA and Battle trials at the SWOG Group Meeting

February 2012 – NCI TMSC, FDA, Leading Academicians, Clinicians, Industry, Government representatives

November 2012 – Lung Master Protocol Trial Design Proposal hosted by Friends of Cancer Research

March 2013 – Development of the Lung Master Protocol

JUNE 2014 – ACTIVATION!

L-R: M. Redman, J. Abrams, V. Miller, A. Ashby, V. Papadimitrakopoulou, D. Gandara, J. Woodcock, R. Herbst, J. Allen

NCI: National Cancer Institute;
TMSC: Thoracic Malignancies Steering Committee
TCGA: The Cancer Genome Atlas

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The Story of Lung-MAP

June 16, 2014 - ACTIVATION

- **Lung Master protocol with an "umbrella" trial design**
  - Evaluation of multiple investigational therapies in independently conducted therapeutic studies
  - Under a single infrastructure
  - "One-stop-shop"
  - Ability to screen large number of patients
- **Opened with 5 treatment sub-studies**
  - 4 biomarker-driven, 1 non-matched

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Original Lung-MAP (S1400) Trial Schema

FMI NGS/MET IHC

S1400A	S1400B	S1400C	S1400D	S1400E
Non-match	PI3K+	CCGA+*	FGFR+	MET+
Anti-PD-L1	*PI3Ki*	CDK4/6i	*FGFRi*	HGF mAb
1:1	1:1	1:1	1:1	1:1
Arm[1] / Arm[2]	Arm[1] / Arm[2]	Arm[1] / Arm[2]	Arm[1] / Arm[2]	Arm[1] / Arm[2]
[1] Medi4736	[1] GDC-0032	[1] Palbociclib	[1] AZD4547	[1] Rilotumumab + erlotinib
[2] Docetaxel	[2] Docetaxel	[2] Docetaxel	[2] Docetaxel	[2] Erlotinib

* Cell cycle gene alteration

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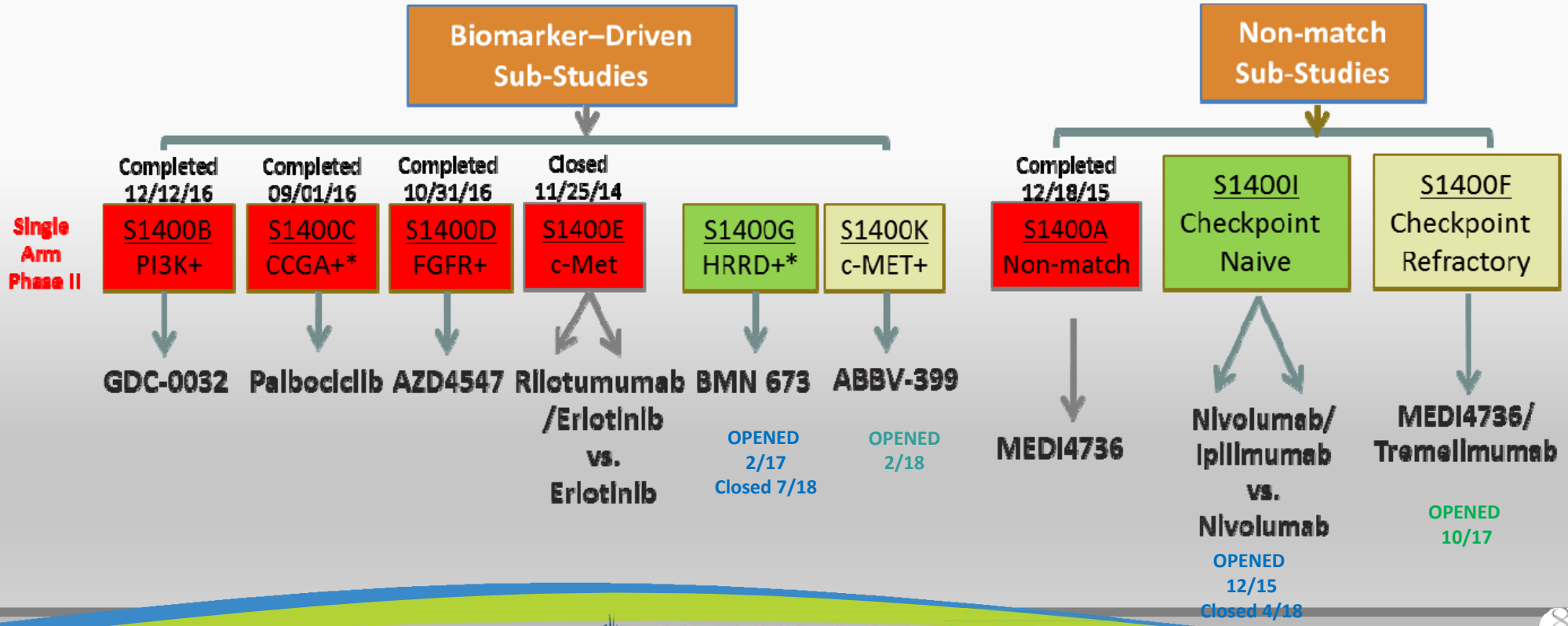
Current Lung-MAP Schema



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Lessons Learned

Master Protocols are Feasible

1. **Unique public-private partnership has been key**
   - A true NCTN effort in both leadership and study conduct (accrual from 427 sites to date)
   - FNIH as the "purse-holder" and contractor is an asset
   - Active engagement of 10 different companies
   - Advocacy partnerships have been essential (Friends as lead)
2. **Master protocol flexibility & adaptation to changes in the therapeutic landscape are essential**
   - "Umbrella" infrastructure & autonomy of each sub-study facilitates opening-closing of new sub-studies quickly ("Self-Sustaining")
   - "Umbrella" infrastructure allowed redesign with the major change of immunotherapy emergence
   - Phase II single arm → randomized Phase II/III design retains FDA approval goal at every stage
   - Re-design to "2nd line and beyond" is consistent with current drug approval paradigms

Where We're Going

PROTOCOL INFRASTRUCTURE

New Trial Structure

Previously-treated Stage IV or Recurrent
Non-Small Cell Lung Cancer
(all histologic types of NSCLC)
Immunotherapy or Chemotherapy Relapsed/Refractory Patients

Biomarker-matched* Sub-studies

Biomarker 1 Positive

Sub-study 1
Biomarker-driven Therapy

Investigational therapy 1

...Biomarker n Positive

...Sub-study n
Biomarker-driven Therapy

Investigational therapy n

Stage 1:

Stage 2:

R

Investigational therapy 1 | Standard of Care

R

Investigational therapy n | Standard of Care

Non-Matched Sub-studies

IO Naïve

No planned studies currently

IO Relapsed/Refractory

S1400F
Durvalumab/ Tremelimumab (squamous only)

Study Activated 10/2017
Accrual on-going

S1800 – immunotherapy combination platform

*Currently, biomarkers are defined by NGS and c-MET IHC screening through Lung-MAP, though approaches such as Immunotherapy biomarkers may be used.

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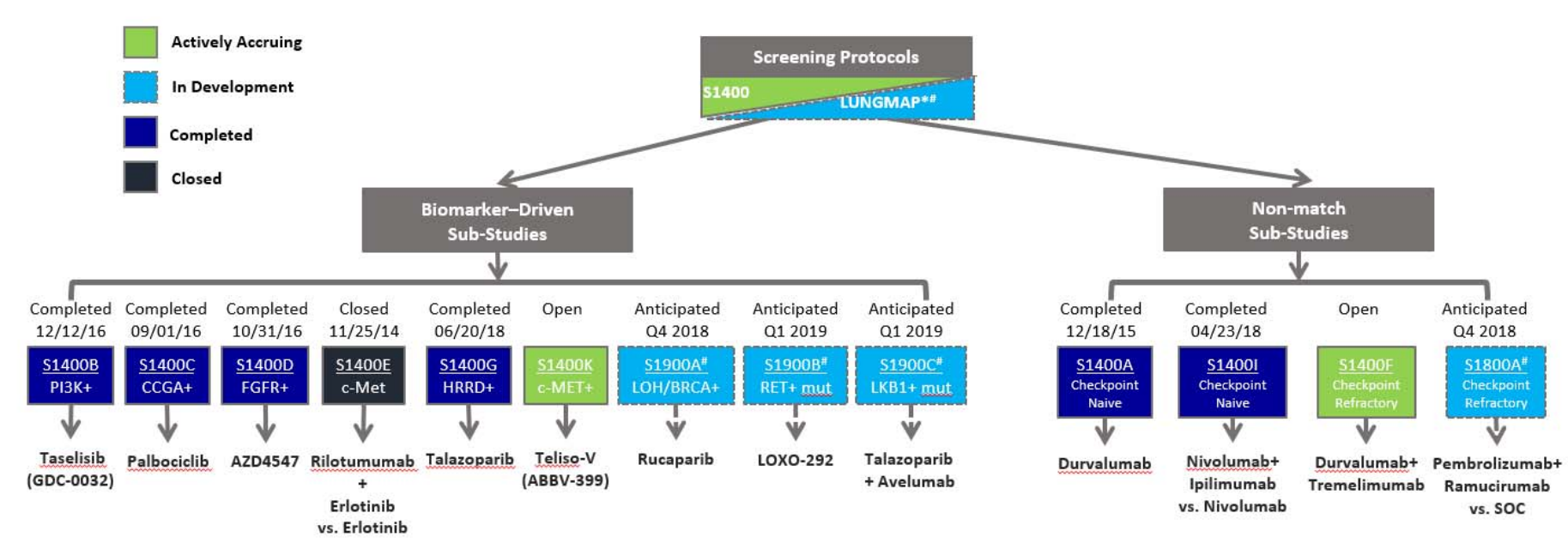
Where We're Going – Current Schema



*The new umbrella screening protocol will simply be referred to as **LungMAP**. It will allow the trial to expand to include all NSCLC histologies and include more patients.

#Only new sub-studies will be open to all NSCLC histologies. The current sub-studies are only for patients with squamous cell carcinoma.

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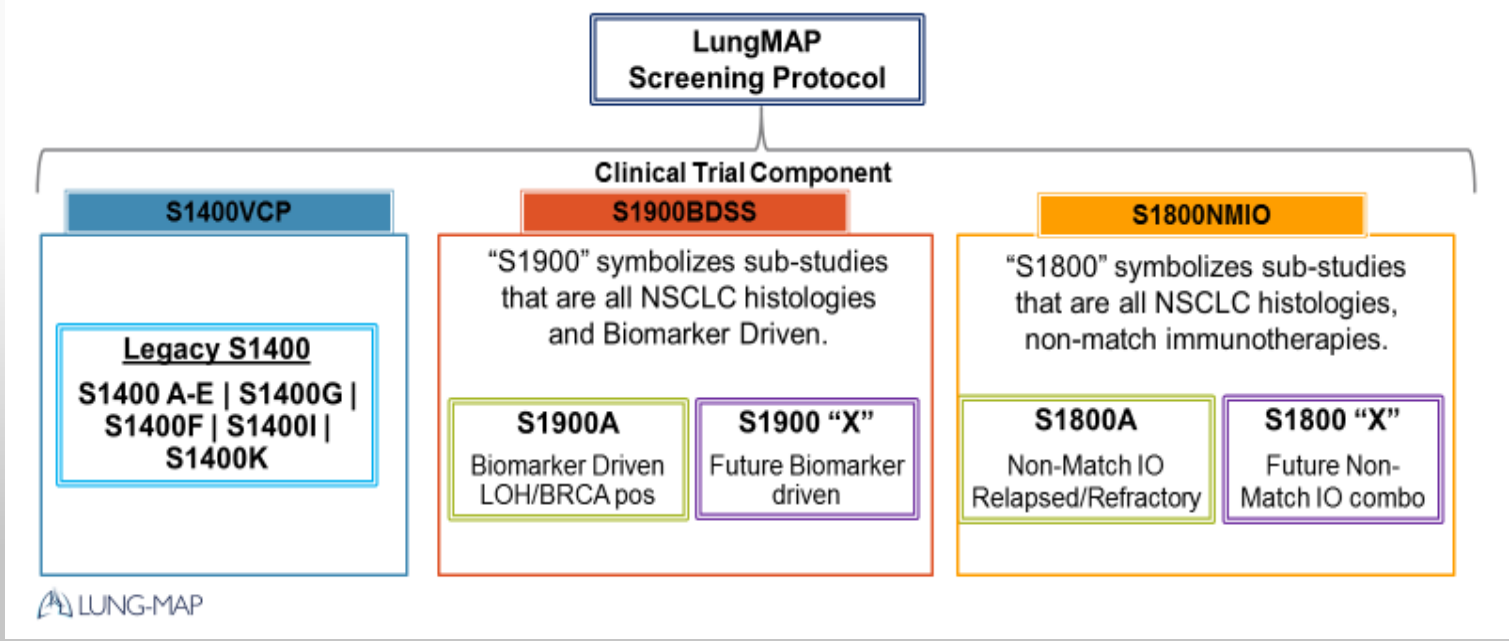
Where We're Going – Protocol Infrastructure

The structure of Lung-MAP has been improved with the expansion

- Stand-alone Protocols
- Set within a defined module
  - Legacy
  - Biomarker-Driven
  - Non-Match



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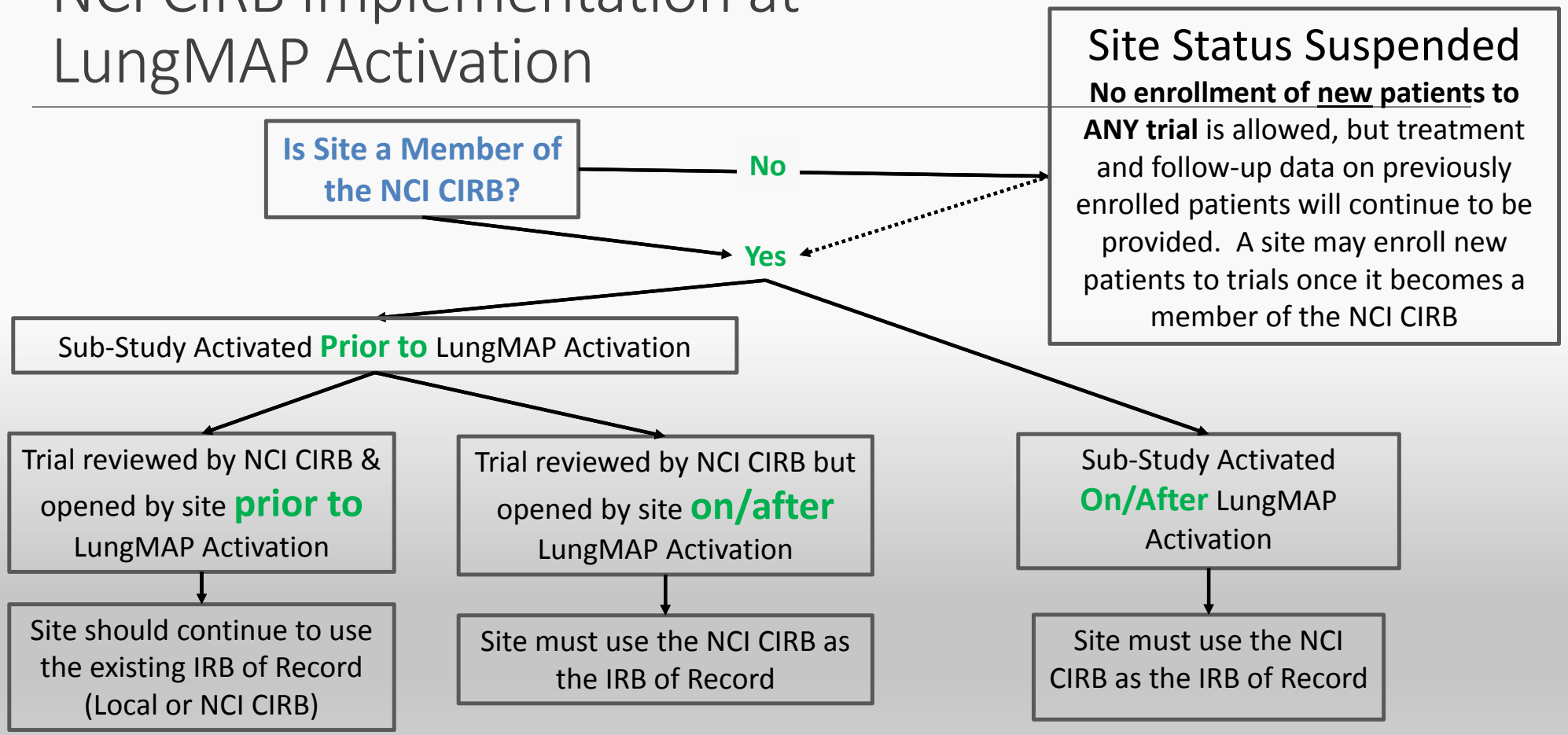
Where We're Going

New Screening Protocol, "LungMAP"

- **LungMAP has been reviewed and approved by CTEP and CIRB. Awaiting approval of sub-study S1900A.**
  - S1400 will close to accrual when LungMAP activates
  - addition of liquid biopsies
  - streamlined informed consent form that combines screening and prescreening – a step that will make it easier to enroll patients.
- **CIRB Membership mandate** to comply with the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research.
  - another move to speed the process of opening the trial at sites and registering patients.

NCI CIRB Implementation at LungMAP Activation



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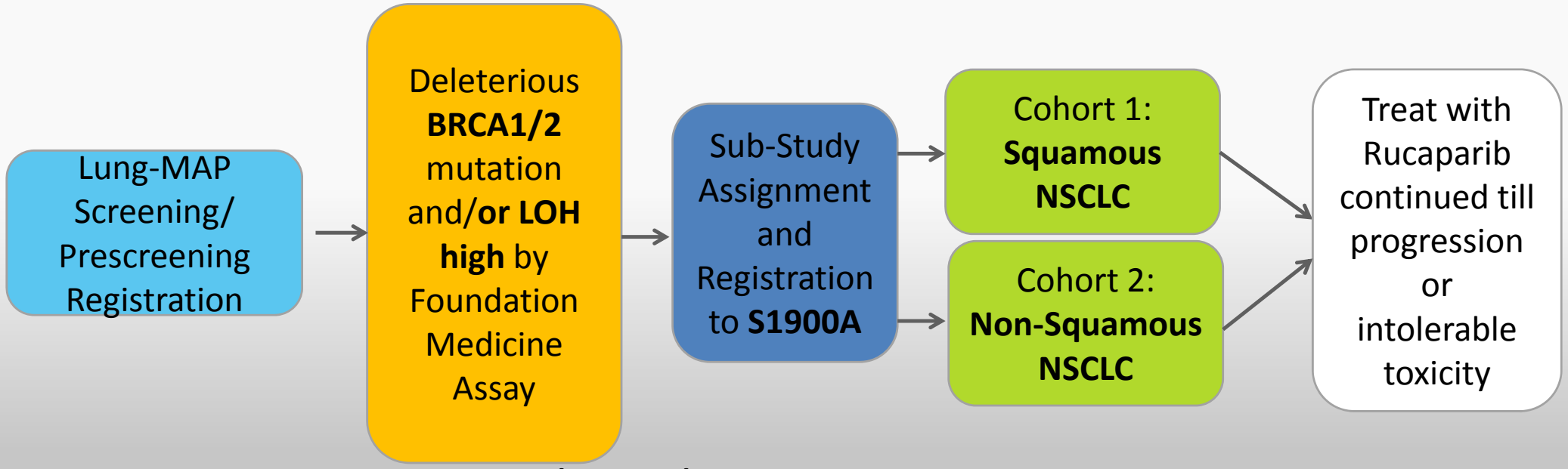
Where We're Going

SUB-STUDIES

Reporting on Completed Sub-studies

- S1400A-D – reported at ASCO 2017, manuscripts expected to be submitted for publication soon
- S1400 common manuscript – expected to be submitted for publication soon
- S1400G – to be submitted for ASCO 2019 and primary manuscript within year
- S1400I – to be submitted for ASCO 2019 and primary manuscript within year

S1900A: A PHASE II STUDY OF RUCAPARIB IN PATIENTS WITH GENOMIC LOH HIGH AND/OR DELETERIOUS BRCA1/2 MUTATION STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER (LUNG-MAP SUB-STUDY) PI Reiss



Accrual goal: 44 patients per cohort (88 total)
Activated: TBD (CIRB review – 10/4/18)
Goal: >10 responses per cohort

Go to:
http://www.swogstat.org/accrual/lungmap.pdf
for current status

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S1800A - A PHASE II RANDOMIZED STUDY OF RAMUCIRUMAB PLUS MK3475 (PEMBROLIZUMAB) VERSUS STANDARD OF CARE FOR PATIENTS PREVIOUSLY TREATED WITH IMMUNOTHERAPY FOR STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER (LUNG-MAP NON-MATCHED SUB-STUDY) PI RECKAMP, DRAGNEV

Anticipated Open Q4 2018

Registration to S1400/LUNGMAP

Screening study to determine sub-study assignment

Randomization

ARM A
Investigator's Choice
Standard of Care

ARM B
Ramucirumab plus MK-3475
(Pembrolizumab)

Eligibility Criteria

- NSCLC
- Stage IV or Recurrent
- Previously treated with chemo and immunotherapy

Primary Objective

Compare overall survival in patients randomized to ramucirumab and MK3475 vs. standard of care

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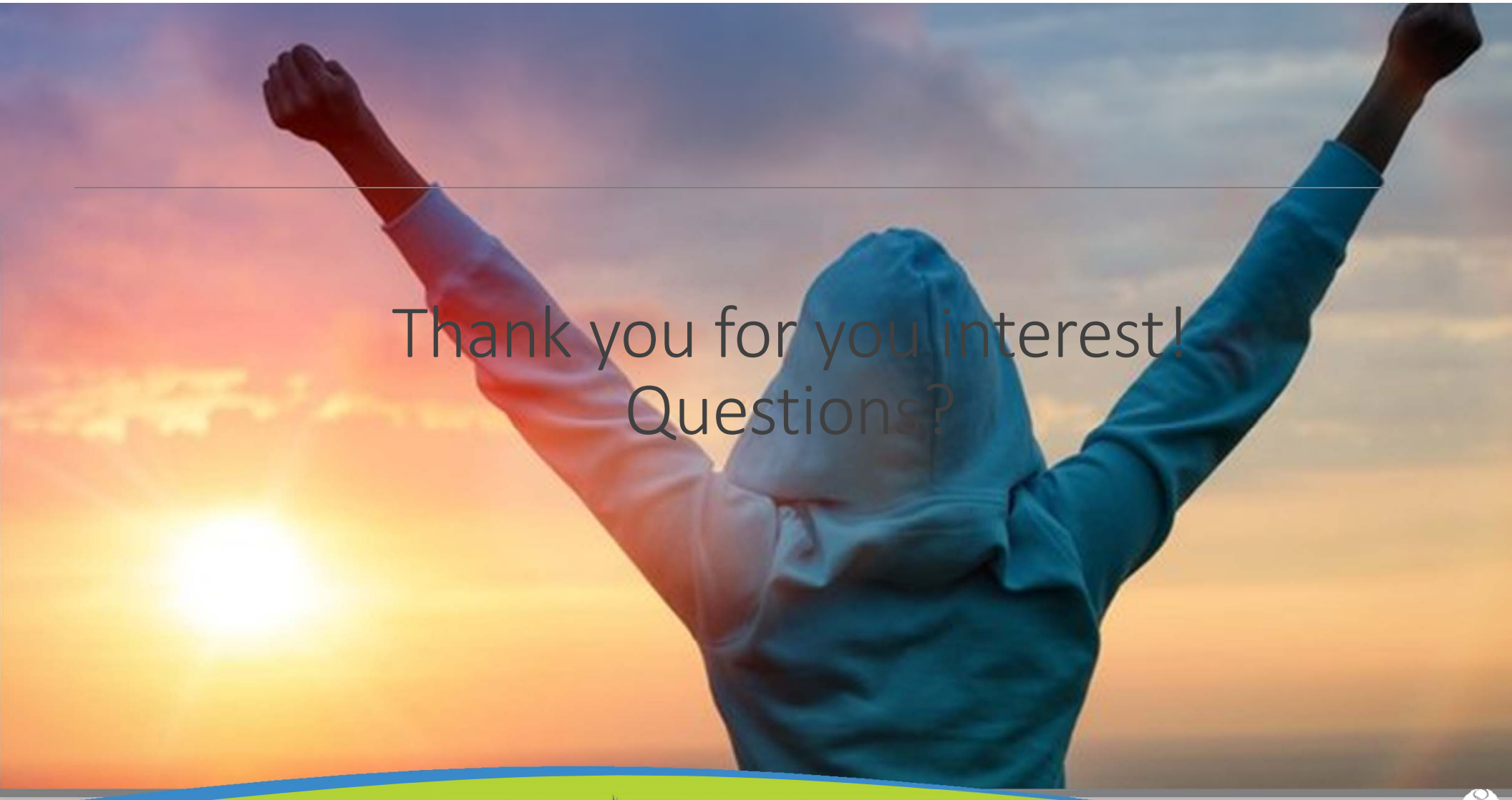
Additional Sub-studies in Development

- **S1900B**
  - testing RET mutated tumors
  - LOXO-292
  - Single Arm Phase II registration trial
- **S1900C**
  - testing STK11/LKB1 mutated tumors
  - Avelumab and talazoparib
  - Single arm Phase II signal seeking trial

- **Other studies in development**



Thank you for you interest! Questions?

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