# Array BioPharma

**February 5, 2019**

**> Second Quarter F2019 Update**

# SAFE HARBOR STATEMENT

Forward-looking statements made in the course of this presentation are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The audience is cautioned that such forward looking statements involve risks and uncertainties, including those described in our annual report filed on form 10-K for the year ended June 30, 2018, and other filings of the company with the Securities and Exchange Commission, which may cause the company's actual results and experience to differ materially from anticipated results and expectations expressed in these forward-looking statements.

BRAFTOVI® capsules in combination with MEKTOVI® tablets is approved in the U.S. for the treatment of patients with unresectable or metastatic melanoma with a *BRAF*$^{V600E}$ or *BRAF*$^{V600K}$ mutation, as detected by an FDA-approved test. BRAFTOVI is not indicated for the treatment of patients with wild-type BRAF melanoma. Encorafenib and binimetinib are not approved for use in any other disease state. COLUMBUS and BEACON trial safety data are available the Array BioPharma website at www.arraybiopharma.com. Important Safety Information, as well as full U.S. prescribing information at www.braftovimektovi.com or: http://www.arraybiopharma.com/documents/Braftovi_Prescribing_information.pdf and http://www.arraybiopharma.com/documents/Mektovi_Prescribing_information.pdf

# Maximizing Success of Encorafenib & Binimetinib is Array's Top Priority

FDA and EC Approved BRAFTOVI® (encorafenib) + MEKTOVI® (binimetinib)

| SIGNIFICANT MILESTONES ACHIEVED… | …WITH IMPORTANT UPCOMING VALUE DRIVERS |
|---|---|
| **BRAFTOVI + MEKTOVI launched in US*** | |
| • Positive reception from U.S. melanoma healthcare providers<br>• **$22.7 million net product sales** in second commercial quarter<br>• **>2,600 TRx** in second commercial quarter; **~4,000 TRx to date** | • **Continued penetration in melanoma** |
| **BRAFTOVI + MEKTOVI approved in Europe for advanced *BRAF*-mutant melanoma** | • **European commercial expansion** |
| ***BRAF*-MUTANT METASTATIC CRC (mCRC)** | |
| • BEACON CRC Safety Lead-in at ASCO GI: **15.3 months mature median OS**<br>• FDA granted Breakthrough Therapy Designation<br>• Planned interim analysis after consultation with FDA and EMA; analysis for U.S. sNDA based primarily on ORR and duration of response | • **Enrollment completed**<br>• **Plan to seek accelerated approval in the U.S. if supported by positive interim results**<br>• **Topline results 1H19** |
| **Binimetinib + Encorafenib + Cetuximab in First-line *BRAF*$^{V600E}$-mutant mCRC** | • **Currently enrolling** |

**Binimetinib + I/O COLLABORATIONS/MSS CRC AND OTHER CANCERS**

Bristol-Myers Squibb · MERCK · Pfizer

**COST SHARING**

BEACON CRC co-funding: Pierre Fabre (40%), Ono Pharmaceuticals (milestone payments), Merck KGaA (Cetuximab supply)

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# Encorafenib & Binimetinib Well-Positioned for Success

Partnerships with Ono Pharmaceutical & Pierre Fabre Create a Strong Global Footprint

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**Approved in U.S.**

*Other:* *Canada*

Pierre Fabre

**Approved in EUROPE**

*ROW*

ONO PHARMACEUTICAL CO.,LTD.

**Approved in JAPAN**

*South Korea*

| | | |
|---|---|---|
| **Upfront & Milestone Payments:** | $45 million | $40 million |
| **Global Development Co-Funding:** | 40% | 12% |
| **Remaining Milestones:** | $390 million | $149 million* |
| **Royalties:** | Max. 35% above €100M combined annual sales | Max. 25% above ¥10B combined annual sales |

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*Exchange rate as of the most recent quarter end

# Commercial Update

**Andy Robbins, Chief Operating Officer**

# Strong Demand for BRAFTOVI® + MEKTOVI® for *BRAF*-mutant Melanoma


- **Second commercial quarter:**
  - $22.7 million net sales, 62% Q/Q growth
  - >2,600 TRx in second commercial quarter
  - ~4,000 TRx to date
- **Prescribing in both academic and community centers**
  - New prescribers continue to be identified each month
  - ‘Switch’ patients are declining as proportion of new patient starts
- **Product profile continues to be perceived as differentiated**
  - OS, PFS and ORR results compelling
  - Tolerability profile provides new option for patients

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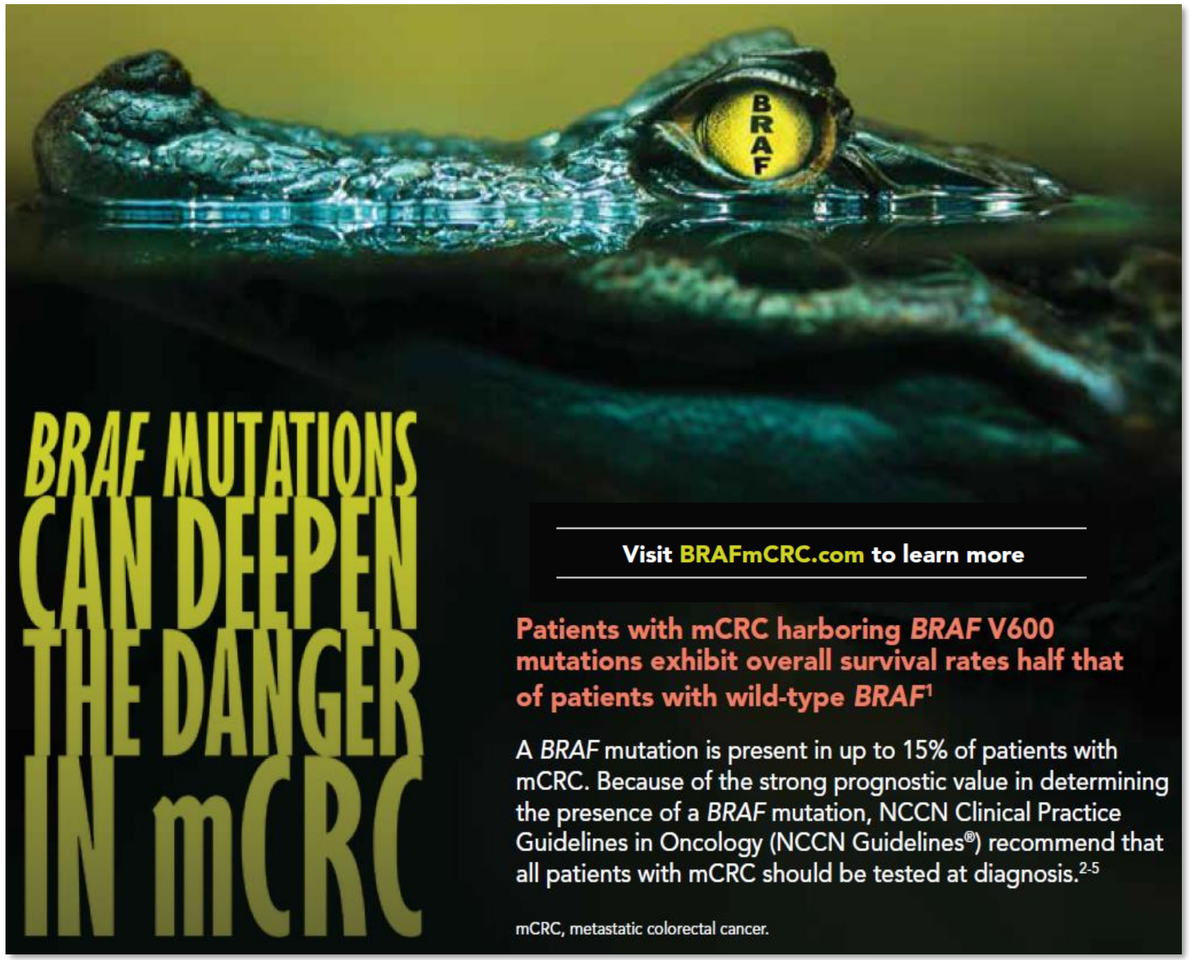
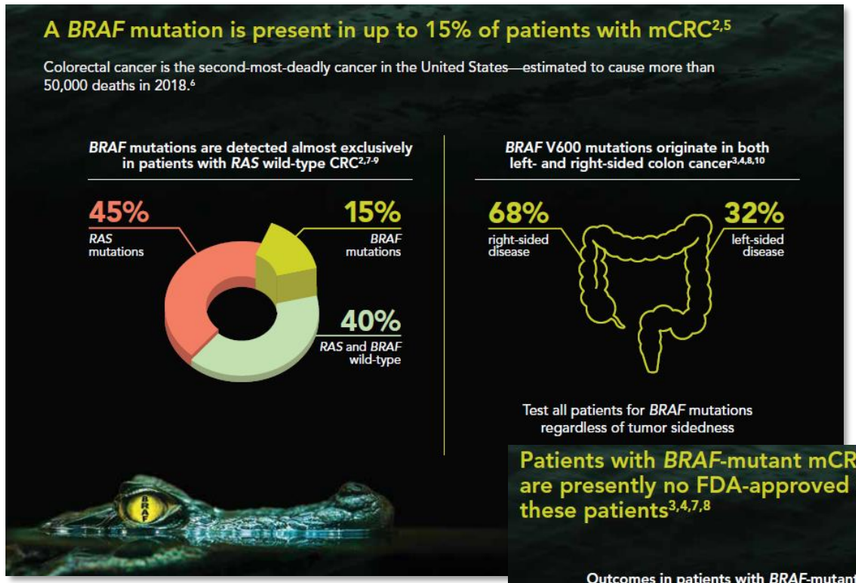
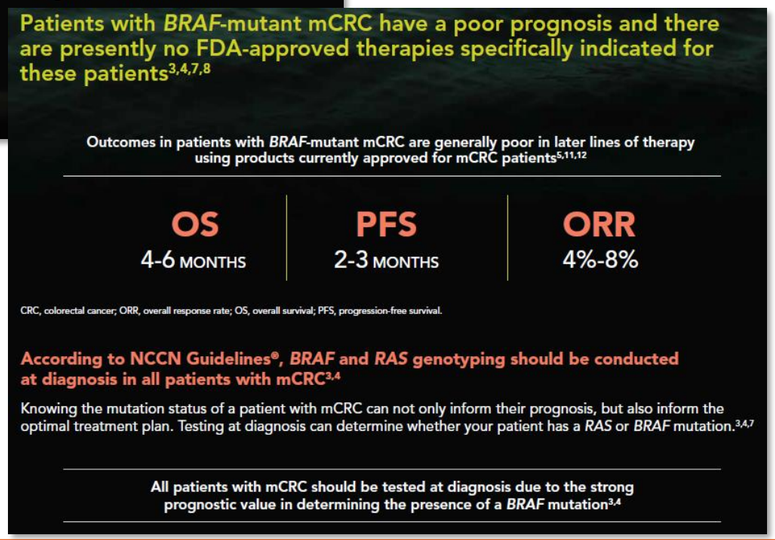
# BRAF CRC Disease Education Campaign Launched



# PHASE 3 *BRAF*-MUTANT CRC TRIAL ADVANCING

## Promising BEACON CRC Safety Lead-In Activity

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# FDA Grants Breakthrough Therapy Designation

Regulatory Update

## BREAKTHROUGH THERAPY DESIGNATION

- FDA has granted Breakthrough Therapy Designation for BRAFTOVI®, in combination with MEKTOVI® and cetuximab for the treatment of patients with *BRAF*$^{V600E}$-mutant mCRC as detected by an FDA-approved test, after failure of one to two prior lines of therapy for metastatic disease.
- Breakthrough Therapy Designation is an FDA process designed to expedite the development and review of drugs that are intended to treat a serious condition where preliminary clinical evidence indicates that they may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints.

## REGULATORY UPDATE

- Topline results anticipated in the first half of 2019
- Initiated amendment to the BEACON CRC protocol to allow for interim analysis following consultation with FDA and EMA, and to seek accelerated approval in the U.S. based on positive results
- Analysis for planned U.S. sNDA based primarily on ORR and duration of response
  - Timing allows for the subset of patients required for the interim analysis of ORR to achieve an objective response and for the durability of responses to be appropriately evaluated.

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# Original Phase 3 *BRAF*-mutant Colorectal Cancer Study Design*

## Potential to Establish BRAF + MEK + EGFR Combination as New Standard of Care

BEACON CRC

Binimetinib, Encorafenib, and Cetuximab Combined to Treat BRAF-mutant Colorectal Cancer

SAFETY LEAD-IN

COMPLETE

Safety and tolerability will be assessed in patients receiving encorafenib, binimetinib and cetuximab for the treatment of $BRAF^{V600E}$-mutant metastatic colorectal cancer
n=30

RANDOMIZED PORTION

Patient population
- $BRAF^{V600E}$-mutant
- >65% 2nd-line patients
- <35% 3rd-line patients

n=615

Enrollment Completed

Randomization

**Triplet Therapy**
Encorafenib + Binimetinib + Cetuximab
n=205

**Doublet Therapy**
Encorafenib + Cetuximab
n=205

**Control Arm**
FOLFIRI + Cetuximab or
Irinotecan + Cetuximab
n=205

DISEASE PROGRESSION

DISEASE PROGRESSION

DISEASE PROGRESSION

Continued follow-up for evaluation of OS

**Primary Endpoint:** Overall survival (OS) of the triplet therapy compared to the control arm
**Secondary Endpoints:** Address efficacy of the doublet therapy compared to the control arm, and the triplet therapy compared to the doublet therapy
**Other Secondary Endpoints:** Progression-free survival (PFS), objective response rate (ORR), duration of response, safety and tolerability. Health related quality of life data will also be assessed

The trial is being conducted at over 200 investigational sites in North America, South America, Europe and the Asia Pacific region.**

***The trial has been amended to include an interim analysis of endpoints including ORR.**

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The use of encorafenib and binimetinib in this disease state is investigational only and has not been approved by the U.S. Food and Drug Administration.
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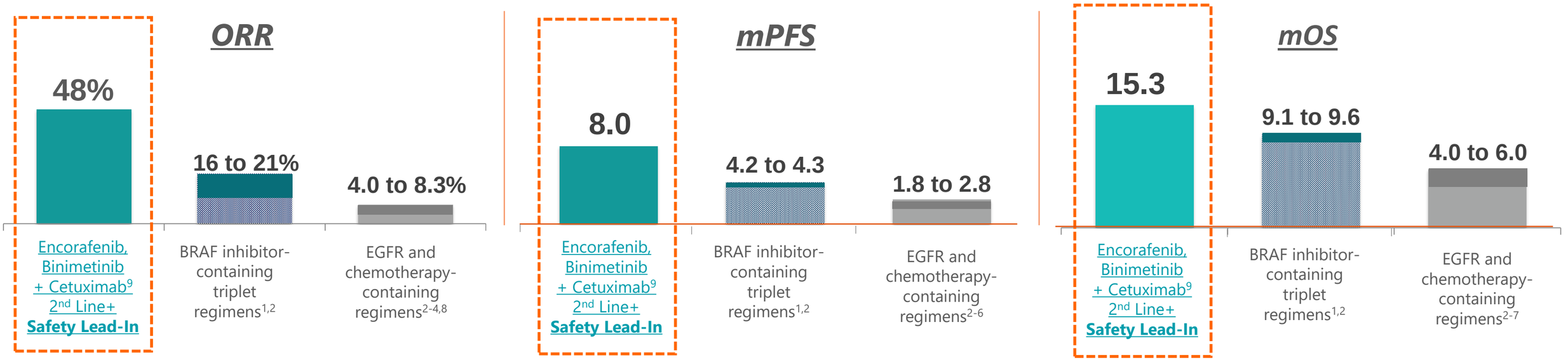
# Observed Clinical Activity from BEACON CRC Safety Lead In and Certain Separate Historical Benchmarks in 2nd Line+ *BRAF*m mCRC

## *2ND Line+ BRAFm mCRC**




**BRAF inhibitor-containing triplet regimens:** dabrafenib, a BRAF inhibitor, trametinib, a MEK inhibitor and panitumumab, a monoclonal EGFR antibody or vemurafenib, a BRAF inhibitor, cetuximab and irinotecan, a chemotherapy

**EGFR inhibitor and chemotherapy-containing regimens:** cetuximab or panitumumab, monoclonal EGFR antibody and chemotherapy including irinotecan

***Array has not conducted head-to-head studies comparing encorafenib and binimetinib against the other BRAF/MEK combination therapies, and these data come from separate Phase 3 and Phase 2 studies. These trials were conducted under varying conditions and results may not be directly comparable.**


1.Corcoran et al., *Cancer Discovery* April 2018 | 2. Kopetz et al., *ASCO 2017* | 3. De Roock et al., *Lancet Oncol, 2010* | 4. Ulivi et al., *J Transl Med. 2012* | 5. Peeters et al., *ASCO 2014* | 6. Saridaki et al., *PLoS One. 2013* | 7. Loupakis et al., *Br J Cancer. 2009* | 8. Seymour et al., Lancet Oncol, 2013 (supplementary appendix) | 9. Kopetz et al, *ASCO GI 2019*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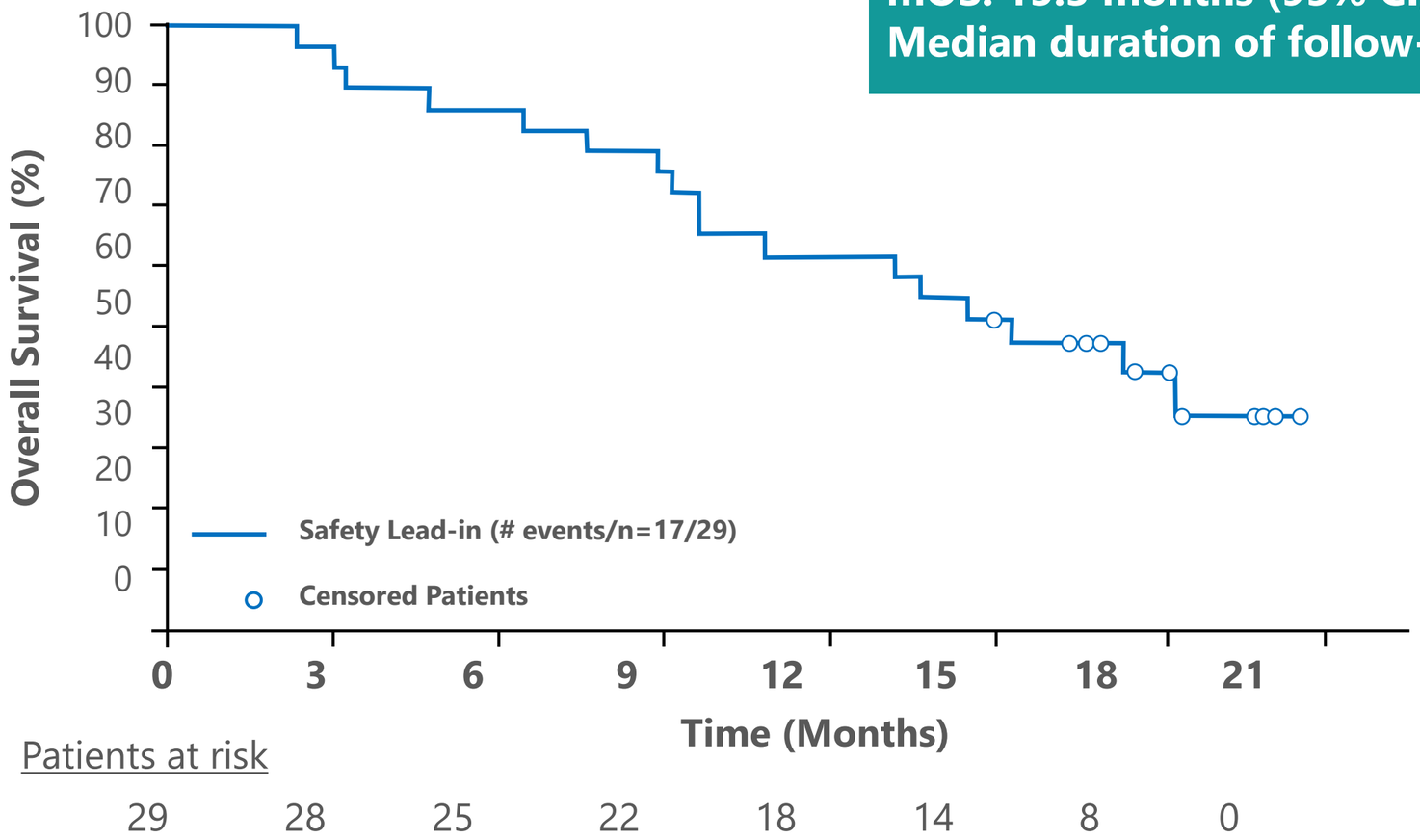
# BEACON CRC Safety Lead-In[1]

## 15.3 Months Median Overall Survival (mOS)

Gastrointestinal Cancers Symposium
Multidisciplinary Treatment, Personalized Care, Optimal Outcomes

**mOS: 15.3 months (95% CI, 9.6-NR)**
**Median duration of follow-up: 18.2 months**




[1]Kopetz et al, ASCO GI 2019; The use of encorafenib and binimetinib in this disease state is investigational only and has not been approved by the U.S. Food and Drug Administration.
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# BEACON CRC Safety Lead-In[1]

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| CONFIRMED BEST OVERALL RESPONSE* | PATIENTS (N=29)** Local Assessment |
|---|---|
| **CR + PR** | **14 (48%)** (95% CI 29%-68%) |
| **CR** | **3 (10%)** |
| **PR** | 11 (38%) |
| **SD** | 13 (45%) |
| **PD** | 0 |
| **DCR** | 27 (93%) |
| **No postbaseline tumor assessments†** | 2 (7) |

- 48% confirmed ORR (CR + PR), (3 complete responses) in patients with *BRAF*$^{V600E}$–mutant mCRC§
  - Overall response rate by central assessment (41%) was consistent with local assessment

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A *BRAF*$^{V600E}$ mutation was identified in 29 patients; 1 treated patient was determined to have a non-*V600 BRAF* mutation (*BRAF*$^{G466V}$) *Locally assessed response per RECIST 1.1; **Patients with BRAF$^{V600E}$ mutations; †Nonresponders per intent-to-treat analysis; CR=complete response; PD=progressive disease; PR=partial response; SD=stable disease; DCR = Disease Control Rate; [1]Kopetz et al, ASCO GI 2019. §ORR by Central Assessment is 41% (95% CI 24%–61%). Encorafenib and binimetinib are not approved for use in CRC. COLUMBUS and BEACON trial safety data are available at www.arraybiopharma.com. Important Safety Information and full U.S. prescribing information available at www.braftovimektovi.com.

# BEACON CRC Safety Lead-In[1]

## Best Percentage Change in Tumor Measurement from Baseline Local Assessment

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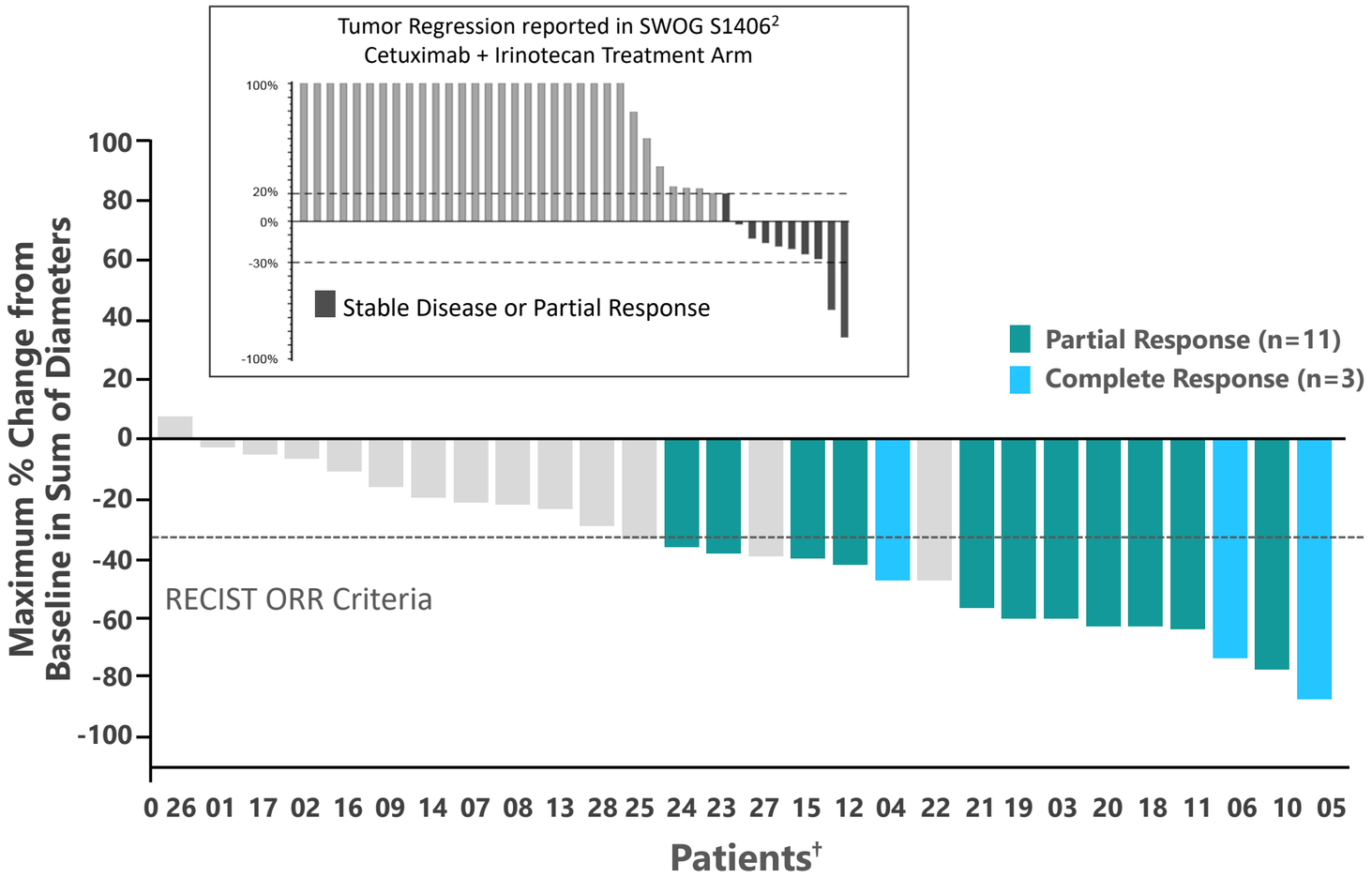


- 27 out of 28 patients with a post-baseline assessment showed tumor regression and none showed RECIST-defined progression as their best response
- mPFS is 8.0 months (95% CI, 5.6–9.3 months)

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mCRC=metastatic colorectal cancer. *Patients with lymph node disease with decreases in short axis dimensions consistent with RECIST 1.1 defined Complete Response.
†One patient had no baseline sum of longest diameters and is not presented. [1]Kopetz et al, ASCO GI 2019.; [2]Kopetz S, et al. *J Clin Oncol.* 2017;35:Abstr 3505, with permission. Encorafenib and binimetinib are not approved for use in CRC. COLUMBUS and BEACON trial safety data are available at www.arraybiopharma.com. Important Safety Information and full U.S. prescribing information available at www.braftovimektovi.com.

# BEACON CRC Safety Lead-In[1]

## Duration on Treatment

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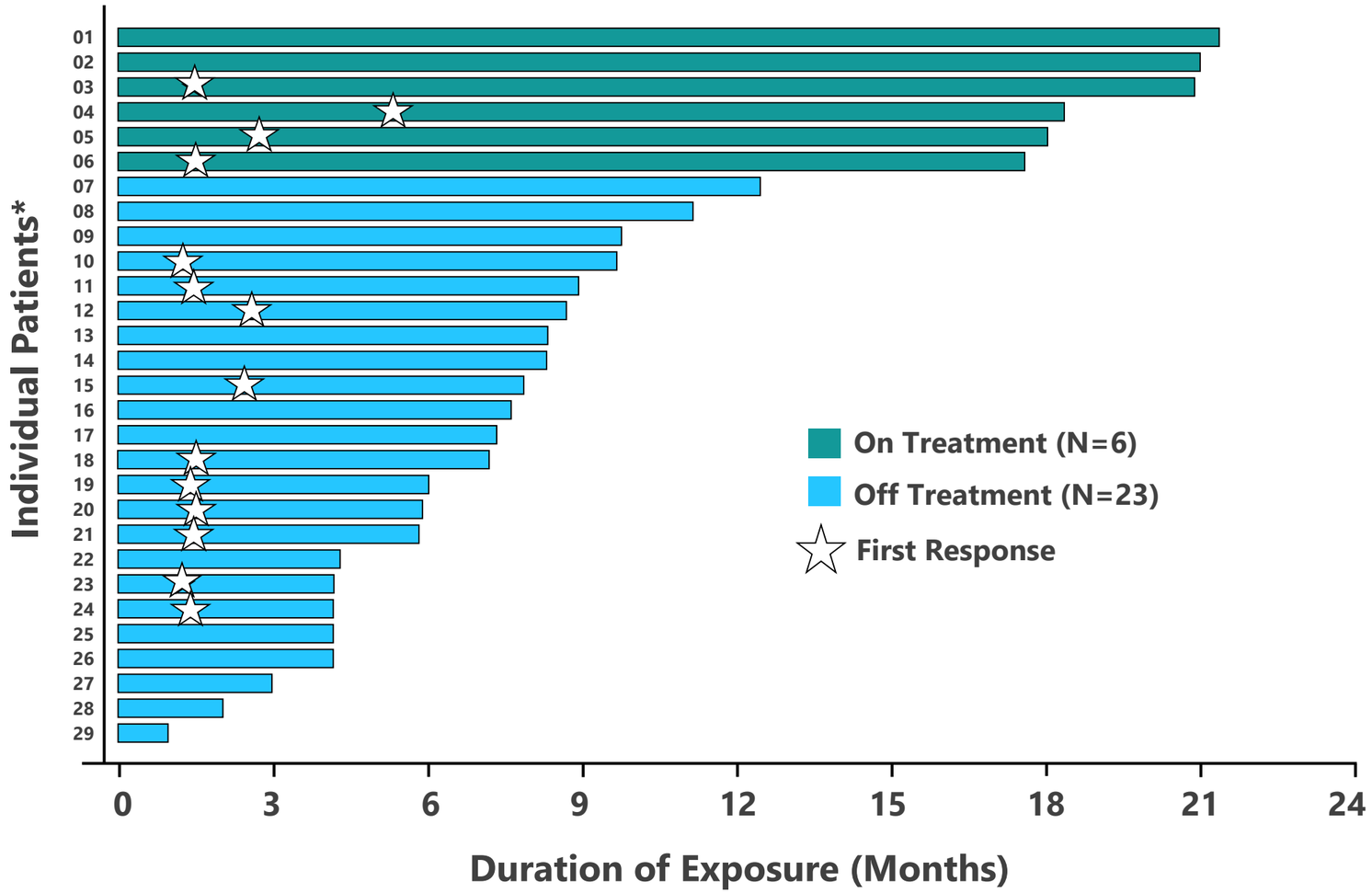


Median time on study treatment[§]:

- 7.9 months (range, 1.0–21.4 months)

Percentage of patients with responses lasting ≥6 months[†]:

- Local assessment: 43%
- Central assessment: 73%

*Patients with BRAF$^{V600E}$ mutations; [1]Kopetz et al, ASCO GI 2019. [§]Median duration of response was 5.5 months (95% CI, 4.1 months–not reached [NR]) per local assessment and 8.2 months (95% CI, 2.8 months–NR) per central assessment. [†]Per Kaplan-Meier estimate

# BEACON CRC Safety Lead-In[1]

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## Safety

| | PATIENTS (N=30) |
|---|---|
| **Adverse Events (AEs)#** | 30 (100%) |
| **Grade 3/4 AEs** | 21 (70%) |
| **AEs leading to discontinuation of all 3 drugs** | 1 (3%) |
| **AEs leading to discontinuation of at least 1 drug*** | 6 (20%) |
| **AEs leading to dose interruption/change†** | 5 (17%) |
| **On-treatment deaths§** | 5 (17%) |

GRADE 3/4 AEs REPORTED IN AT LEAST 10% OF PATIENTS WERE (patients):

- Fatigue (n=4)
- Anemia (n=3)
- Increased blood creatine phosphokinase (CK; n=3)
- Increased aspartate aminotransferase (AST; n=3)
- Urinary tract infections (n=3)

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#DLTs were observed in n=5 of 30 patients included in the safety population, have been reported previously *Includes increased blood bilirubin (1 patient), drug hypersensitivity (1 patient), dyspnea (1 patient), fatigue (1 patient), hypersensitivity (1 patient), malaise (1 patient), retinal detachment (1 patient). †Discontinuation or dose interruption/change of at least one study drug. §Includes on-treatment deaths and deaths within 30 days of stopping study treatment. On-treatment deaths were due to disease progression. [1]Kopetz et al, ASCO GI 2019

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# ANCHOR CRC Trial

## First-line *BRAF*$^{V600E}$–mutant metastatic CRC

# ANCHOR CRC Trial

Encorafenib + Binimetinib + Cetuximab in previously untreated *BRAF*-mutant mCRC


- **Enrolling:** Phase 2, single arm trial in approximately 90 patients with *BRAF*$^{V600E}$-mutant mCRC; no prior therapy for metastatic disease
- **Primary endpoint:** Overall response rate
- **Secondary endpoints:** Duration of response, time to response, progression-free survival, overall survival, quality of life measures, safety, tolerability & pharmacokinetics
- Treatment until disease progression, unacceptable toxicity or consent withdrawal
- Post treatment: Follow-up for survival every 3 months until death or end of trial

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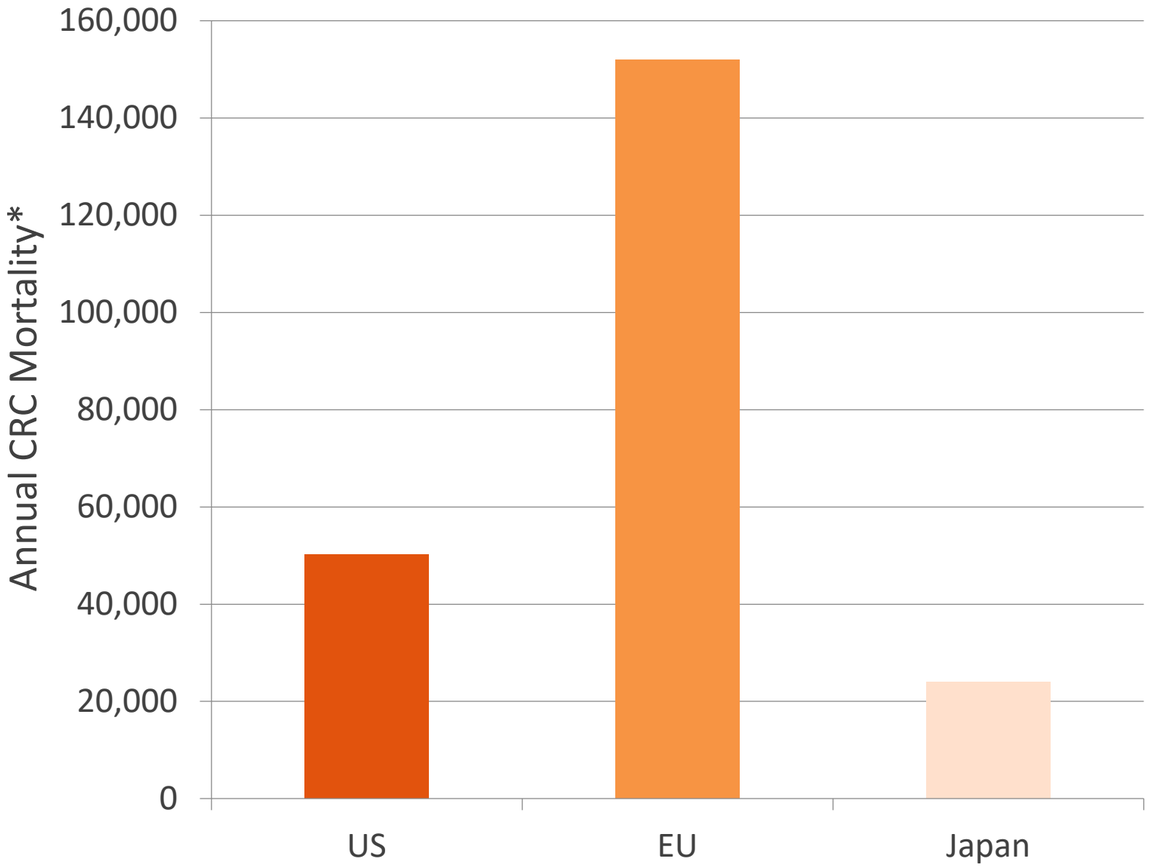
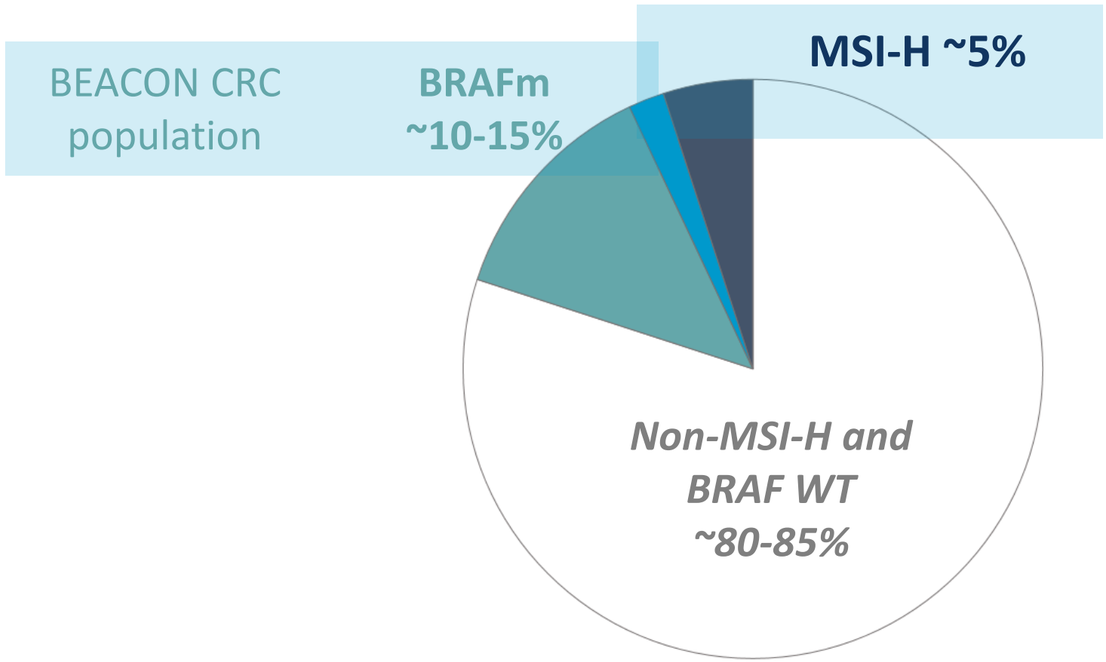
# Global Colorectal Cancer Market

Population Estimates

## ANNUAL COLORECTAL CANCER MORTALITY




## CRC MUTATIONAL SUBGROUPS




*Based on 2018 SEER and 2012 GLOBOCAN epidemiology reports

# STRATEGIC IMMUNO-ONCOLOGY PARTNERSHIPS & PORTFOLIO

# MEK + PD-1/PD-L1 Development Strategy

Collaborations advancing with Bristol-Myers Squibb, Merck & Pfizer

Based on growing body of preclinical & clinical evidence that MEK inhibition may enhance the activity of immunotherapies, Array structured 3 clinical trial collaborations investigating the safety and activity of **binimetinib** with leading checkpoint inhibitors

| **Binimetinib Combo Studies** | Bristol-Myers Squibb | MERCK | Pfizer |
|---|---|---|---|
| **I/O partner** | **Nivolumab (PD-1)** | **Pembrolizumab (PD-1)** | **Avelumab (PD-L1)** |
| **Initial Patient Population** | *RAS*m MSS colorectal cancer | MSS colorectal cancer | Pancreatic cancer & NSCLC |
| **Line Therapy** | 2nd or 3rd line | 1st or 2nd line | 2nd or 3rd line |
| **Trial Sponsor** | Array | Merck | Pfizer |
| **Triple Combination Option (+/-)** | Ipilimumab (CTLA-4) | FOLFOX (Chemo) or FOLFIRI (Chemo) | Talazoparib (PARP) |

# Financials

**Jason Haddock, Chief Financial Officer**

# Second Quarter of Fiscal 2019

## Financial Results

| | Three Months Ended December 31, 2018 | Three Months Ended September 30, 2018 | Increase / (Decrease) | Three Months Ended September 30, 2017 | Increase / (Decrease) |
|---|---|---|---|---|---|
| **Revenue** | | | | | |
| Product sales, net | $ 22,713 | $ 13,993 | $ 8,720 | $ - | $ 22,713 |
| Collaboration and license revenue | 50,924 | 31,028 | 19,896 | 19,823 | 31,101 |
| Reimbursement revenue | 8,912 | 11,889 | (2,977) | 22,395 | (13,483) |
| Total revenue | 82,549 | 56,910 | 25,639 | 42,218 | 40,331 |
| **Operating expenses** | | | | | |
| Cost of goods sold | 786 | 195 | 591 | - | 786 |
| Research and development | 62,120 | 55,550 | 6,570 | 56,329 | 5,791 |
| Selling, general and administrative | 30,473 | 24,890 | 5,583 | 11,607 | 18,866 |
| Total operating expenses | 93,379 | 80,635 | 12,744 | 67,936 | 25,443 |
| **Loss from operations** | (10,830) | (23,725) | 12,895 | (25,718) | 14,888 |
| **Other income (expense)** | | | | | |
| Net interest expense | (532) | (1,056) | 524 | (1,578) | 1,046 |
| Other | - | (30) | 30 | (6,757) | (6,757) |
| Total other income (expense), net | (532) | (1,086) | 554 | (8,335) | 7,803 |
| Income tax expense | - | - | - | - | - |
| **Net loss** | $ (11,362) | $ (24,811) | $ 13,449 | $ (34,053) | $ 22,691 |
| **Net loss per share - basic and diluted** | $ (0.05) | $ (0.12) | $ 0.07 | $ (0.17) | $ 0.12 |

| | December 31, 2018 | September 30, 2018 |
|---|---|---|
| Cash, cash equivalents and marketable securities | $ 478,153 | $ 415,391 |

In thousands, except per share data

# Value Drivers

# Maximizing Success of Encorafenib & Binimetinib is Array's Top Priority

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# THANK YOU

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# Appendix

# BRAFTOVI® capsules in combination with MEKTOVI® tablets

## Important Safety Information

**Warnings and Precautions**

**New Primary Malignancies:** Cutaneous and non-cutaneous malignancies can occur. In the COLUMBUS trial, cutaneous squamous cell carcinoma, including keratoacanthoma, occurred in 2.6% and basal cell carcinoma occurred in 1.6% of patients. Perform dermatologic evaluations prior to initiating treatment, every 2 months during treatment, and for up to 6 months following discontinuation of treatment. Manage suspicious skin lesions with excision and dermatopathologic evaluation. Dose modification is not recommended for new primary cutaneous malignancies. Based on its mechanism of action, BRAFTOVI may promote malignancies associated with activation of *RAS* through mutation or other mechanisms. Monitor patients receiving BRAFTOVI for signs and symptoms of non-cutaneous malignancies. Discontinue BRAFTOVI for *RAS* mutation-positive non-cutaneous malignancies.

**Tumor Promotion in BRAF Wild-Type Tumors:** Confirm evidence of *BRAF*$^{V600E}$ or $^{V600K}$ mutation prior to initiating BRAFTOVI.

**Cardiomyopathy,** manifesting as left ventricular dysfunction associated with symptomatic or asymptomatic decreases in ejection fraction, has been reported in patients. In the COLUMBUS trial, cardiomyopathy occurred in 7% and Grade 3 left ventricular dysfunction occurred in 1.6% of patients. Cardiomyopathy resolved in 87% of patients. Assess left ventricular ejection fraction by echocardiogram or MUGA scan prior to initiating treatment, 1 month after initiating treatment, and then every 2 to 3 months during treatment. Safety has not been established in patients with a baseline ejection fraction that is either below 50% or below the institutional lower limit of normal. Patients with cardiovascular risk factors should be monitored closely.

**Venous Thromboembolism (VTE):** In the COLUMBUS trial, VTE occurred in 6% of patients, including 3.1% of patients who developed pulmonary embolism.

**Hemorrhage:** In the COLUMBUS trial, hemorrhage occurred in 19% of patients and ≥ Grade 3 hemorrhage occurred in 3.2% of patients. Fatal intracranial hemorrhage in the setting of new or progressive brain metastases occurred in 1.6% of patients. The most frequent hemorrhagic events were gastrointestinal, including rectal hemorrhage (4.2%), hematochezia (3.1%), and hemorrhoidal hemorrhage (1%).

**Ocular Toxicities:** In the COLUMBUS trial, serous retinopathy occurred in 20% of patients; 8% were retinal detachment and 6% were macular edema. Symptomatic serous retinopathy occurred in 8% of patients with no cases of blindness. RVO is a known class-related adverse reaction of MEK inhibitors and may occur in patients treated with MEKTOVI in combination with encorafenib. In patients with *BRAF* mutation-positive melanoma across multiple clinical trials, 0.1% of patients experienced retinal vein occlusion (RVO). The safety of MEKTOVI has not been established in patients with a history of RVO or current risk factors for RVO including uncontrolled glaucoma or a history of hyperviscosity or hypercoagulability syndromes. Perform ophthalmological evaluation for patient-reported acute vision loss or other visual disturbance within 24 hours. Permanently discontinue MEKTOVI in patients with documented RVO. In COLUMBUS, uveitis, including iritis and iridocyclitis was reported in 4% of patients. Assess for visual symptoms at each visit. Perform ophthalmological evaluation at regular intervals and for any visual disturbances, and to follow new or persistent ophthalmologic findings.

# BRAFTOVI® capsules in combination with MEKTOVI® tablets

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**Interstitial Lung Disease (ILD):** ILD, including pneumonitis occurred in 0.3% of patients with BRAF mutation-positive melanoma across multiple clinical trials. Assess new or progressive unexplained pulmonary symptoms or findings for possible ILD.

**Hepatotoxicity:** In the COLUMBUS trial, the incidence of Grade 3 or 4 increases in liver function laboratory tests was 6% for alanine aminotransferase (ALT) and 2.6% for aspartate aminotransferase (AST), and 0.5% for alkaline phosphatase. Monitor liver laboratory tests before and during treatment and as clinically indicated.

**Rhabdomyolysis:** In the COLUMBUS trial, elevation of laboratory values of serum creatine phosphokinase (CPK) occurred in 58% of patients. Rhabdomyolysis was reported in 0.1% of patients with BRAF mutation-positive melanoma across multiple clinical trials. Monitor CPK and creatinine levels prior to initiating MEKTOVI, periodically during treatment, and as clinically indicated.

**QTc Prolongation:** BRAFTOVI is associated with dose-dependent QTc interval prolongation in some patients. In the COLUMBUS trial, an increase in QTcF to > 500 ms was measured in 0.5% (1/192) of patients. Monitor patients who already have or who are at significant risk of developing QTc prolongation. Correct hypokalemia and hypomagnesemia prior to and during BRAFTOVI administration. Withhold, reduce dose, or permanently discontinue for QTc > 500 ms.

**Embryo-Fetal Toxicity:** BRAFTOVI or MEKTOVI can cause fetal harm when administered to pregnant women. BRAFTOVI can render hormonal contraceptives ineffective. Non-hormonal contraceptives should be used during treatment and for at least 30 days after the final dose for patients taking BRAFTOVI + MEKTOVI.

**Adverse Reactions**
The most common adverse reactions (≥20%, all Grades, in the COLUMBUS trial): were fatigue, nausea, diarrhea, vomiting, abdominal pain, arthralgia, myopathy, hyperkeratosis, rash, headache, constipation, visual impairment, serous retinopathy.

In the COLUMBUS trial, the most common laboratory abnormalities (≥20%, all Grades): included increased creatinine, increased CPK, increased gamma glutamyl transferase, anemia, increased ALT, hyperglycemia, increased AST, and increased alkaline phosphatase.

**Drug Interactions**
Avoid concomitant use of strong or moderate CYP3A4 inhibitors or inducers and sensitive CYP3A4 substrates with BRAFTOVI. Modify BRAFTOVI dose if concomitant use of strong or moderate CYP3A4 inhibitors cannot be avoided. Avoid co-administration of BRAFTOVI with medicinal products with a known potential to prolong QT/QTc interval.