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# Pioneering Bispecific Antibodies

MCLA-128 Presented Data and Program Update

October 28, 2019

# Disclaimer

This presentation (including any oral commentary that accompanies this presentation) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the impact our Biclonics® platform can have on cancer, our product candidates' potential to treat certain types of tumors, our collaborators, the timing of regulatory filings and the timing and anticipated data read outs or results from our clinical trials. These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding, which may not be available and which may require us to restrict out operations or require us to relinquish rights to our technologies or bispecific antibody candidates; potential delays in regulatory approval, which would impact our ability to commercialize our product candidates and affect our ability to generate revenue; the unproven approach to therapeutic intervention of our Biclonics® technology; our limited operating history; economic, political, regulatory and other risks involved with international operations; the lengthy and expensive process of clinical drug development, which has an uncertain outcome; the unpredictable nature of our early stage development efforts for marketable drugs; potential adverse public reaction to the use of cancer immunotherapies; potential delays in enrollment of patients, which could affect the receipt of necessary regulatory approvals; failure to obtain marketing approval internationally; failure to compete successfully against other drug companies; potential competition from other drug companies if we fail to obtain orphan drug designation or maintain orphan drug exclusivity for our products; our reliance on third parties to conduct our clinical trials and the potential for those third parties to not perform satisfactorily; our reliance on third parties to manufacture our product candidates, which may delay, prevent or impair our development and commercialization efforts; protection of our proprietary technology; our patents being found invalid or unenforceable; potential lawsuits for infringement of third-party intellectual property; our ability to attract and retain key personnel; managing our growth could result in difficulties; and we may lose our foreign private issuer status and incur significant expenses as a result.

These and other important factors discussed under the caption “Risk Factors” in our Annual Report on Form 20-F filed with the Securities and Exchange Commission, or SEC, on April 3, 2019, and our other reports filed with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.



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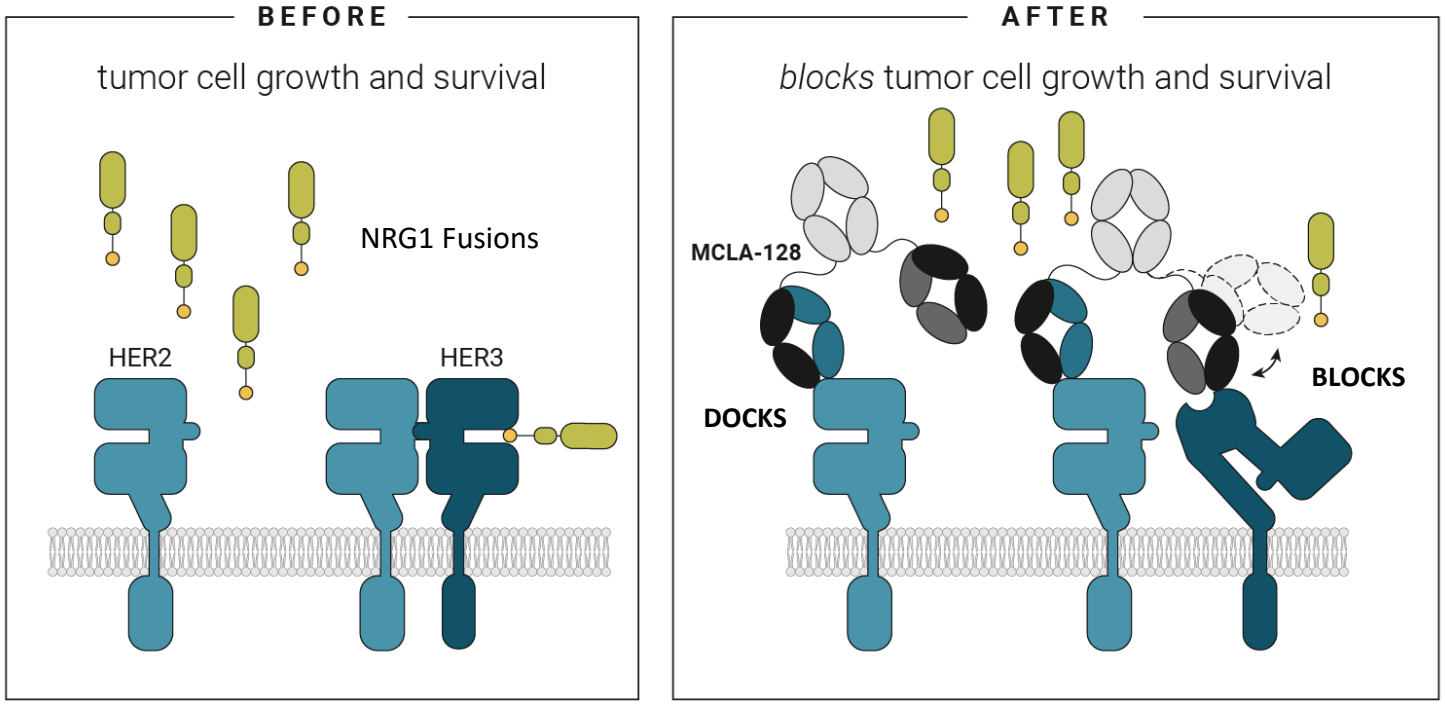
# MCLA-128 update key takeaways

- Demonstrated early clinical proof of concept in pancreatic and lung cancer patients harboring NRG1 Fusions
- Very well tolerated safety profile
- Unique ‘Dock and Block®’ mechanism of action and enhanced ADCC to inhibit the neuregulin/HER3 pathway in solid tumors harboring NRG1 Fusions
- Going forward, Merus plans to focus efforts on MCLA-128 program in Phase 1/2 eNRGy trial for patients with cancer harboring NRG1 Fusions

## May be Uniquely Suited to Target NRG1 Fusions



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# MCLA-128 Dock & Block MOA and NRG1 Fusions



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# MCLA-128 blocks primary tumor cell growth and escape to HER2/EGFR targeted therapy

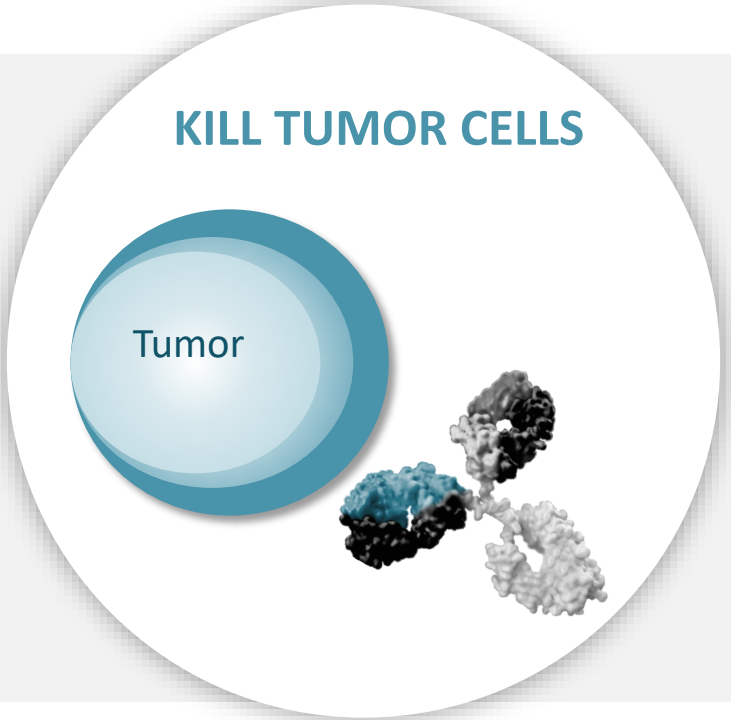
## Unique DOCK & BLOCK® mechanism of action potently inhibits neuregulin (NRG)-driven tumor growth

**Block HER3**

Blocks HER3 signaling even in high neuregulin tumor environments

**Enhanced ADCC**

Mediates tumor elimination by immune killer cells




**Dock HER2**

Docks to HER2 expressed on tumor cells to efficiently block HER2:HER3 dimer formation

**Combination Capable**

Combinations with HER2 targeted therapies possible



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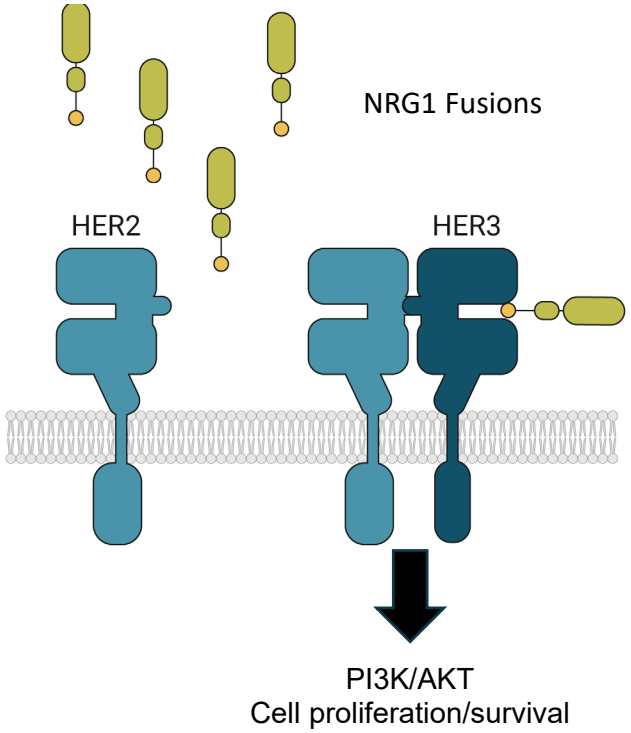
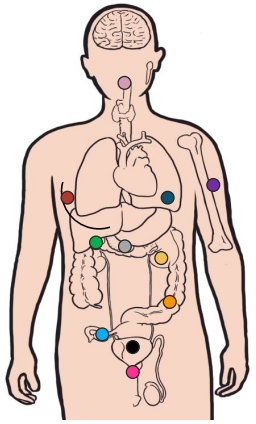
# MCLA-128 may offer a novel therapeutic paradigm for *NRG1* Fusion-positive cancers

## NRG1 FUSIONS STIMULATE TUMOR CELL GROWTH



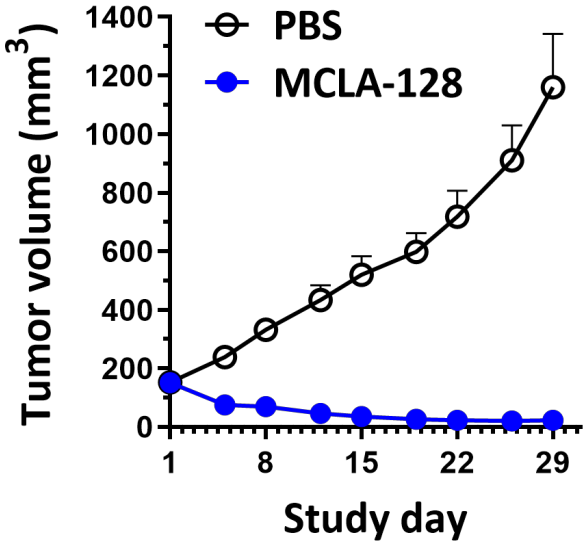

## NRG1 FUSIONS ARE FOUND ACROSS MULTIPLE SOLID TUMOR TYPES



- Lung
- Breast
- Kidney
- Gallbladder
- Pancreas
- Prostate
- Ovarian
- Sarcoma
- Bladder
- Colorectal
- Nasopharyngeal

| Tumor type | Estimated Incidence (%) |
|---|---|
| Lung | 0.3 – 3.0 |
| Pancreas | 0.5 – 1.5 |
| Other | < 1.0 |

## MCLA-128 BLOCKS TUMOR GROWTH IN NRG1 FUSION PDX MODEL




Projections of NRG1 Fusions occurrence (incidence) are based on limited published information



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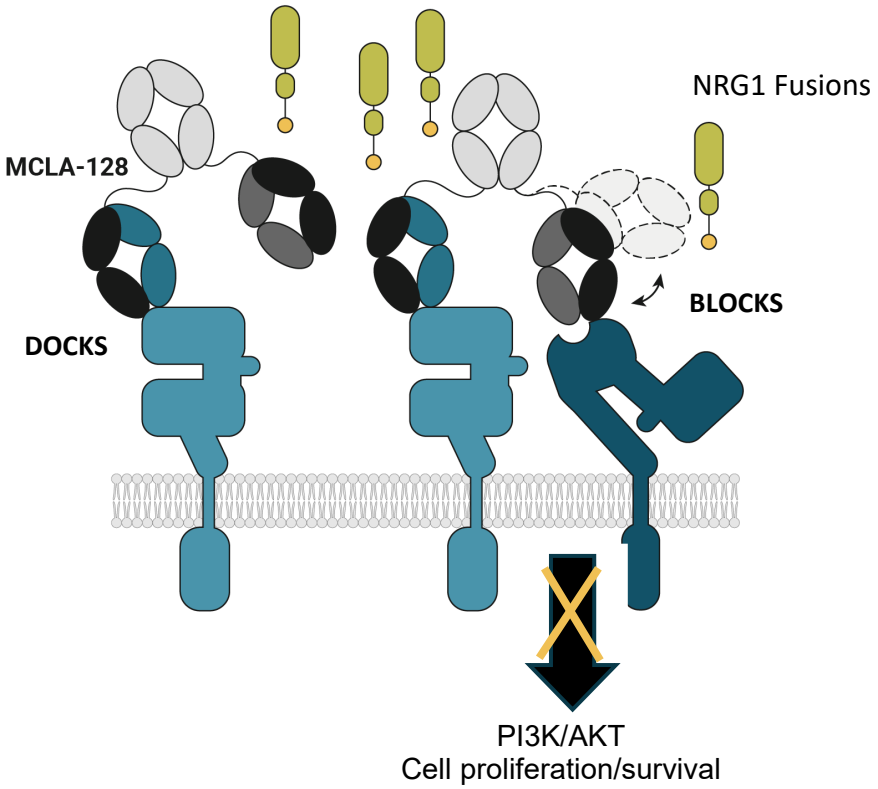
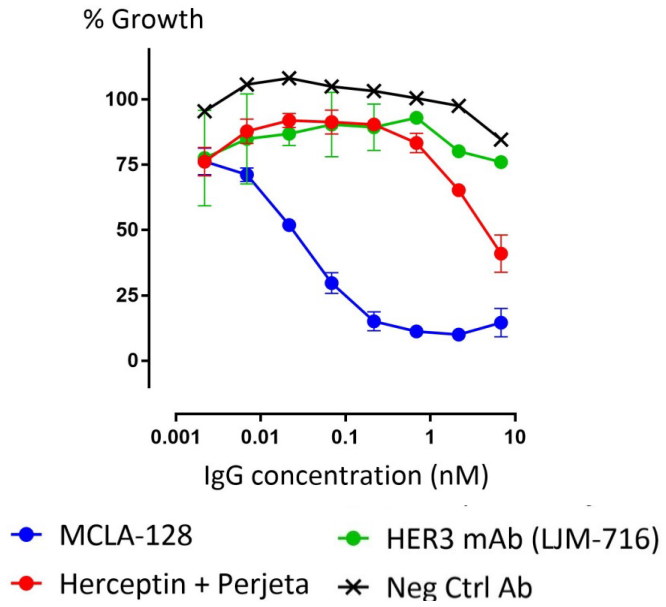
# MCLA-128 efficacy demonstrated in preclinical assays, well-tolerated in patients

## DOCK ONTO HER2 & BLOCK NRG1 -DRIVEN HER/HER3 DIMER FORMATION




## SUPERIOR ACTIVITY SHOWN IN PRECLINICAL MODELS




## SAFETY AND TOLERABILITY IN PHASE 1/2 TRIAL

**117 PATIENTS EVALUATED***

MCLA-128 Dosing: 750 mg ranging from q1w-q3w

- Single agent well tolerated
- Low risk for immunogenicity

Please Refer to https://merus.nl/publications/ for full data presented. Refer to ASCO poster 2018 and AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics 2019

* As of Jan. 2019



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# Memorial Sloan Kettering Presented EAP Data on MCLA-128

**AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics 2019**



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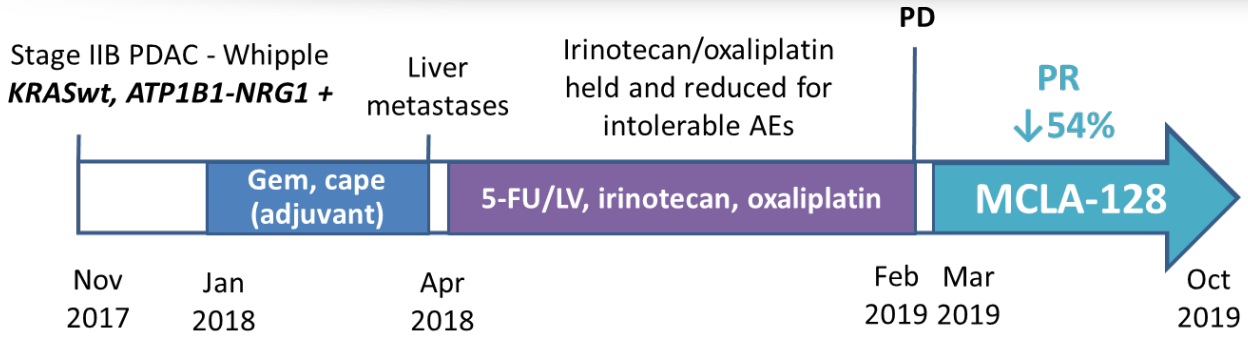
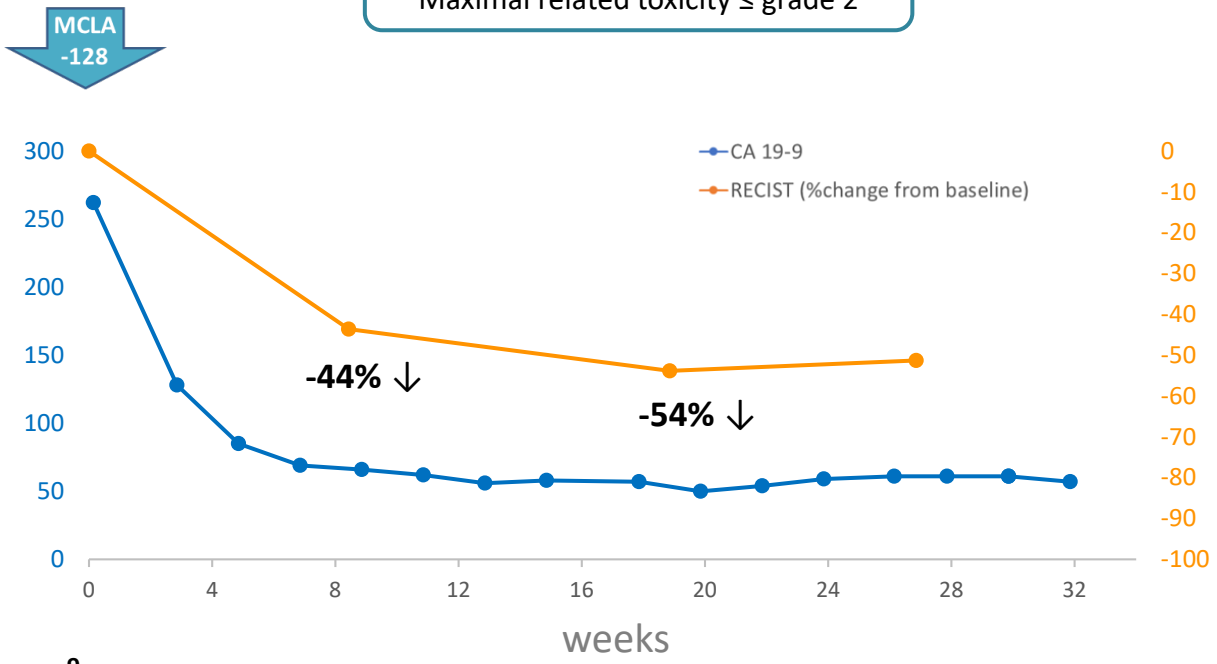
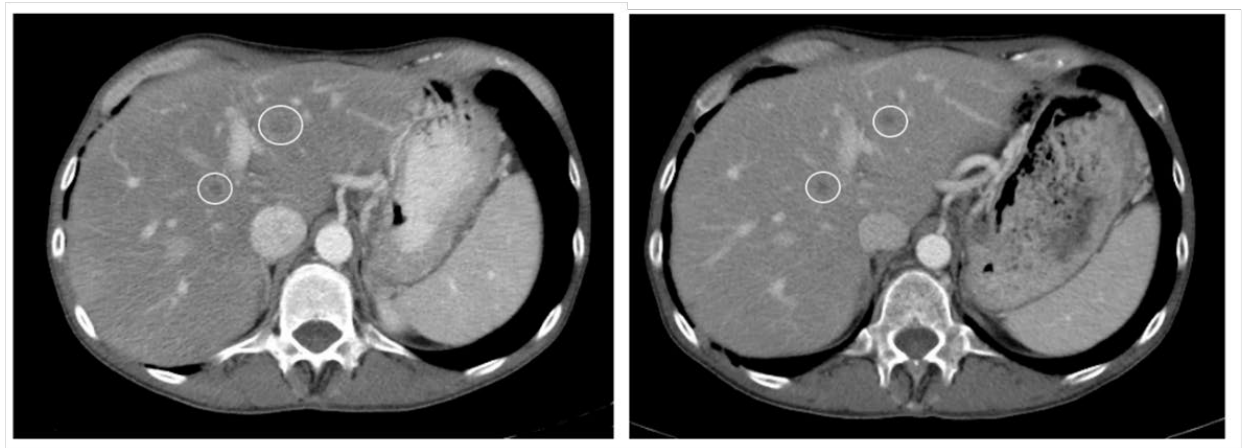
# 52-year-old male with *ATP1B1-NRG1* pancreatic CA



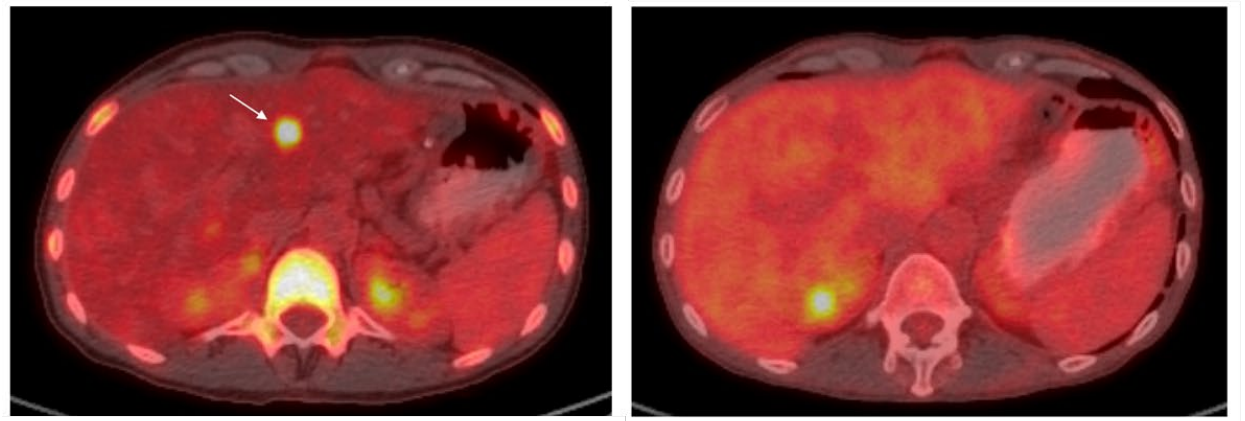

7+ months MCLA-128, 750 mg IV, q2w
Maximal related toxicity ≤ grade 2



Baseline CT

8 week CT



Baseline PET

8 week PET



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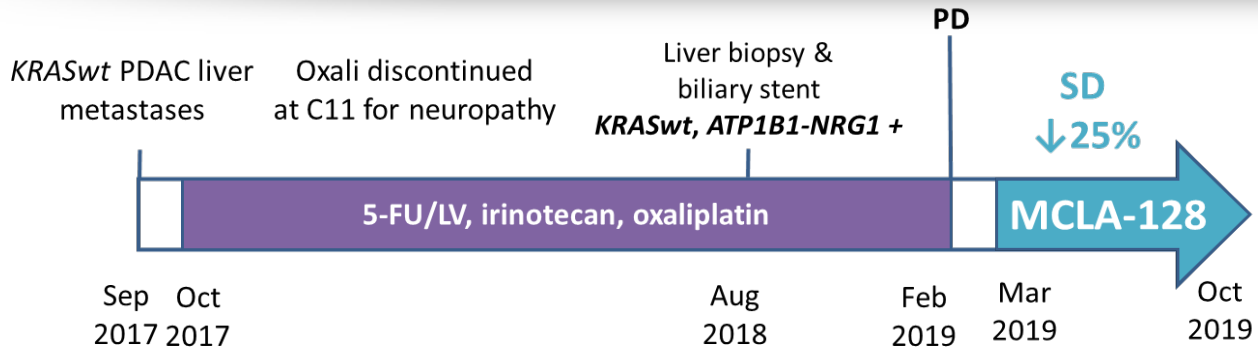
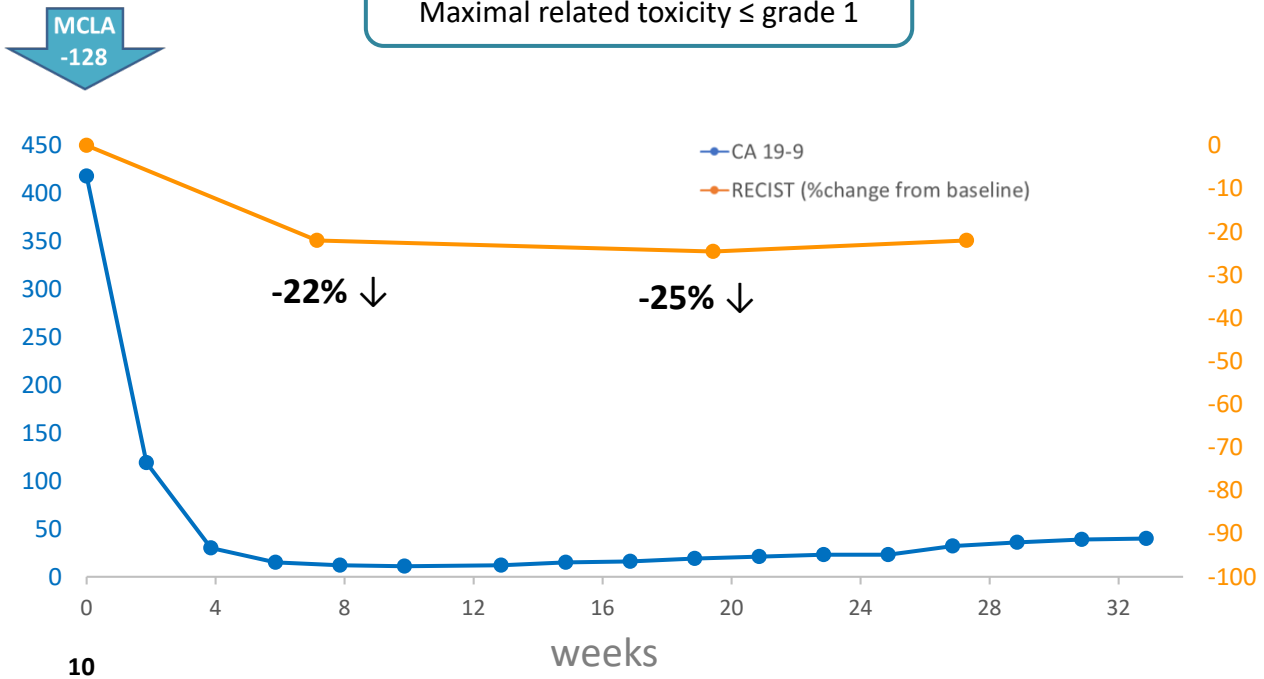
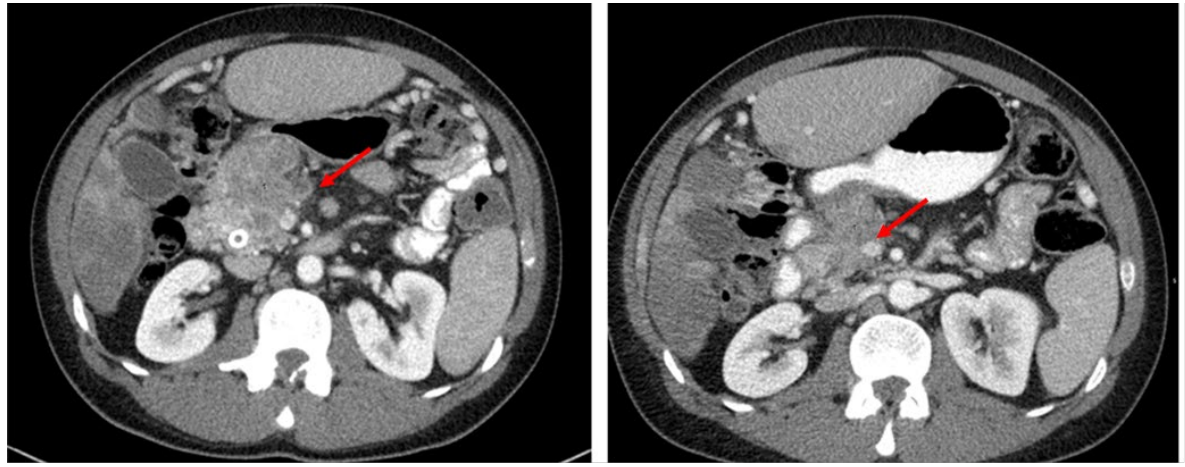
# 34-year-old male with *ATP1B1-NRG1* pancreatic CA

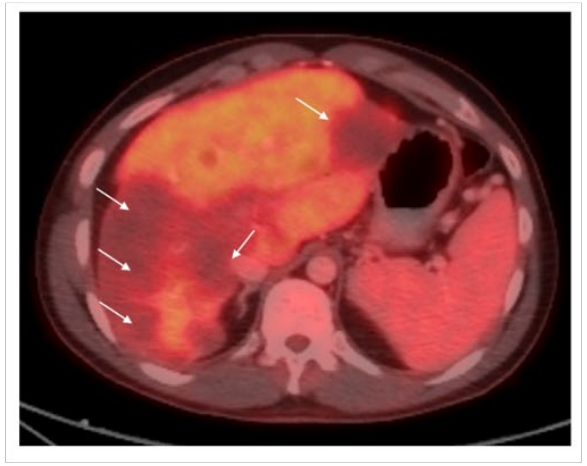



7+ months MCLA-128, 750 mg IV, q2w
Maximal related toxicity ≤ grade 1



**Baseline CT** **7 week CT**



**10 week PET**

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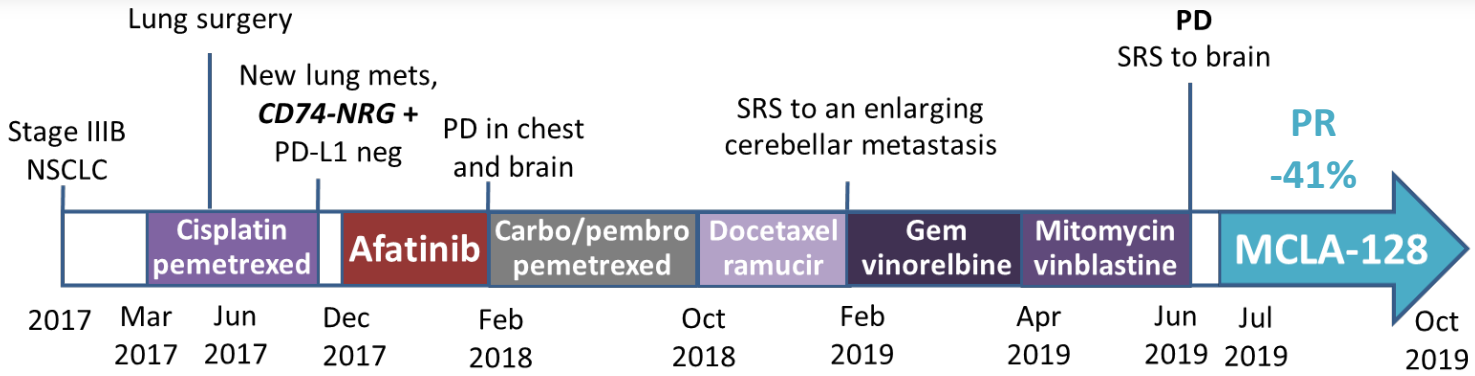
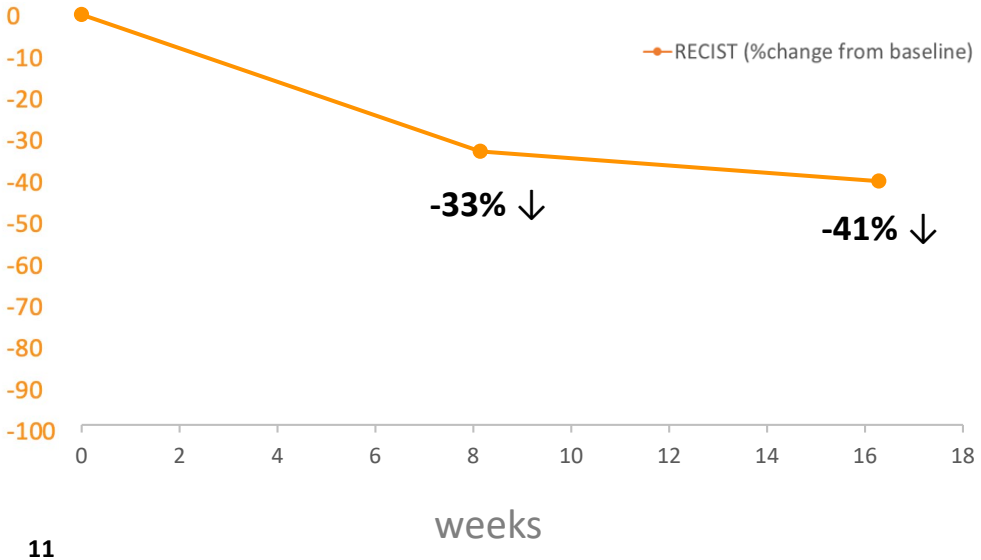
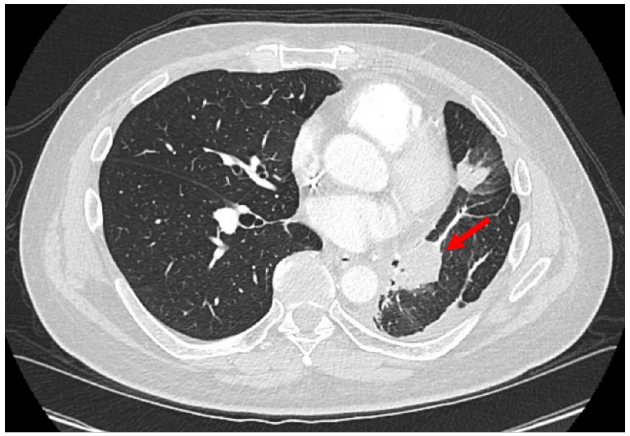
# 54-year-old male with *CD74-NRG1* NSCLC

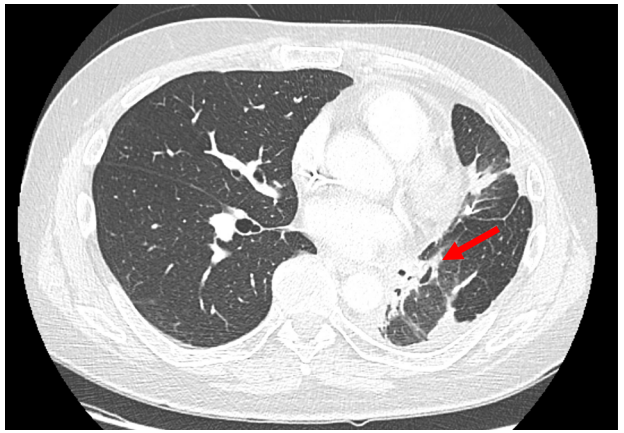



4.5+ months MCLA-128, 750 mg IV, q2w
Maximal related toxicity ≤ grade 1



Baseline



Week 16



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# MCLA-128: well tolerated safety profile

## AEs at RP2D (N=117)

| | AEs irrespective (>7.5% patients) | | AEs related (>2% + >G3) | |
|---|---|---|---|---|
| | All grades | G3* | All grades | G3* |
| ≥1 adverse event | 109 (93.2) | 43 (36.8) | 67 (57.3) | 5 (4.3) |
| Diarrhea | 35 (29.9) | 1 (0.9) | 22 (18.8) | 0 |
| Asthenia | 27 (23.1) | 3 (2.6) | 10 (8.5) | 1 (0.9) |
| Anemia | 22 (18.8) | 4 (3.4) | 1 (0.9) | 0 |
| Nausea | 20 (17.1) | 0 | 10 (8.5) | 0 |
| Fatigue | 18 (15.4) | 2 (1.7) | 8 (6.8) | 0 |
| Vomiting | 17 (14.5) | 0 | 3 (2.6) | 0 |
| Decreased appetite | 15 (12.8) | 1 (0.9) | 6 (5.1) | 0 |
| Dyspnea | 15 (12.8) | 7 (6.0) | 2 (1.7) | 1 (0.9) |
| Hypomagnesaemia | 14 (12.0) | 1 (0.9) | 0 | 0 |
| Constipation | 12 (10.3) | 0 | 1 (0.9) | 0 |
| Cough | 12 (10.3) | 1 (0.9) | 2 (1.7) | 1 (0.9) |
| Abdominal pain | 11 (9.4) | 0 | 2 (1.7) | 0 |
| ALT increased | 10 (8.5) | 4 (3.4) | 0 | 0 |
| AST increased | 10 (8.5) | 4 (3.4) | 0 | 0 |
| Abdominal pain upper | 9 (7.7) | 0 | 0 | 0 |
| IRR | 9 (7.7) | 2 (1.7) | 9 (7.7) | 2 (1.7) |
| Pyrexia | 6 (5.1) | 0 | 3 (2.6) | 0 |
| Myalgia | 5 (4.3) | 1 (0.9) | 3 (2.6) | 1 (0.9) |
| Mucosal inflammation | 5 (4.3) | 0 | 4 (3.4) | 0 |
| Chills | 4 (3.4) | 0 | 4 (3.4) | 0 |
| Hypersensitivity** | 4 (3.4) | 0 | 4 (3.4) | 0 |
| Stomatitis | 3 (2.6) | 0 | 3 (2.6) | 0 |

- 117 patients treated with single-agent MCLA-128 at the RP2Ds in the ongoing phase 2 study (750 mg q3w; 800+400 mg weekly)*
- Most suspected related AEs were grade 1-2, with grade 3 in <5% of patients and no grade 4 related events**
- No severe related gastrointestinal or skin toxicity, nor clinically significant LVEF decreases or cardiac AEs

* Data cut off: Jan-2019.

** 3 patients (2.6%) each had 1 grade 4 unrelated AE; no patients had grade 4 related AEs. A 71-year-old patient had a grade 5 hypersensitivity reaction followed by cardiorespiratory arrest (*Alsina et al. ESMO. 2018 #664P*). The patient's baseline cardiac condition (severe aortic stenosis) contributed to the fatal outcome.



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# MCLA-128 Program Update



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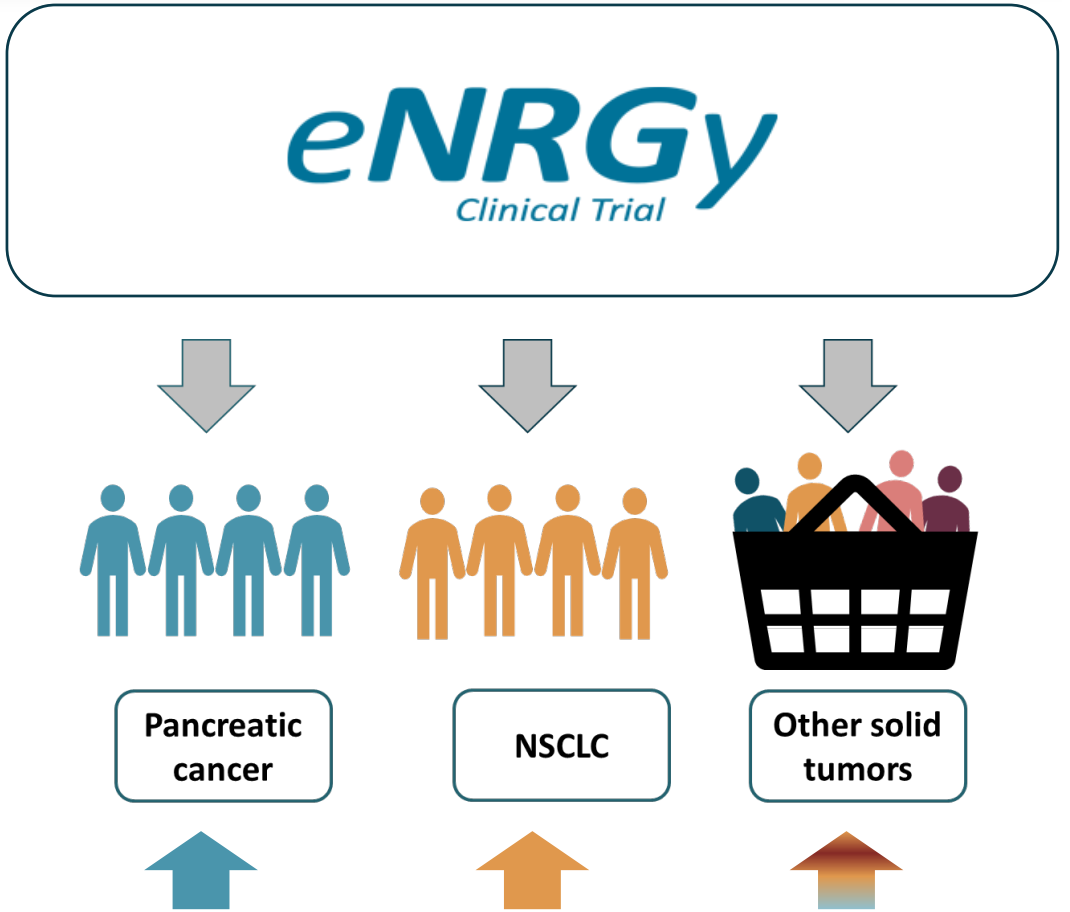
# MCLA-128 activity and durability experience to date with *NRG1* Fusion-positive cancers

| Patient | EAP or Clinical Trial | Treatment duration | Status | Response by RECIST 1.1 | Post-afatinib |
|---|---|---|---|---|---|
| 1 (PDAC) | EAP (MSK) | 7+ months | Ongoing | PR (-54%) | |
| 2 (PDAC) | EAP (MSK) | 7+ months | Ongoing | SD (-25%) | |
| 3 (PDAC) | EAP | n/a | Discontinued* | Not evaluable | |
| 4 (NSCLC) | eNRGy Trial | Too early | Ongoing | Too early for assessment | |
| 5 (NSCLC) | eNRGy Trial | Too early | Ongoing | Too early for assessment | |
| 6 (NSCLC) | eNRGy Trial | n/a | Progressed | PD | |
| 7 (NSCLC) | eNRGy Trial | n/a | Progressed | PD | |
| 8 (NSCLC) | eNRGy Trial | Approx. 7 months | Discontinued** | SD | YES |
| 9 (NSCLC) | EAP (MSK) | Approx. 5 months | Ongoing | PR (-41%) | YES |

*** PDAC Patient 3** received two treatments with MCLA-128 at an approximately four-week non-standard interval due to severity of the illness, and was non-evaluable, passing away due to complications related to the underlying disease prior to first tumor evaluation.
**** NSCLC Patient 8** discontinued the trial due to poor adherence to treatment prot(unrelated to any AE or lack of efficacy)



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# MCLA-128 Metastatic breast cancer Phase 2 combination trial update

## KEY TAKEAWAYS

- No plans to advance into a Phase 3 study in metastatic breast cancer or gastric cancer in the absence of a collaborator
- ER+ cohort is now closed to accrual, >40 patients enrolled
- Merus plans to continue to enroll another approximately 10 patients to reach target accrual in the Her2+ cohort
- Expect to present mature Phase 2 results at medical conference in 2020
  - Primary endpoint of clinical benefit rate at 24 weeks for both cohorts

## MCLA-128 MBC INTERIM EFFICACY ANALYSIS

| | HER2+ cohort | ER+/HER2$^{low}$ cohort |
|---|---|---|
| # patients treated | 24 | 40 |
| Median # of prior lines in metastatic setting | 3 | 2 |
| Visceral involvement, % | 71 | 85 |
| Estimated DCR, % | 75 | 40 |
| Estimated ORR, % | 4 (confirmed)<br>17 (unconfirmed) | 0 |

- Enrollment as of August 31, 2019. Data cut off October 23, 2019
- 100% of the patients in HER2+ cohort received prior trastuzumab, pertuzumab, HER2-directed antibody drug conjugate
- 100% of the patients in ER+/HER2$^{low}$ cohort received prior CDK4/6 inhibitor
- DCR (Disease Control Rate) is defined as the proportion of patients at first assessment who have achieved complete response, partial response and/or stable disease as the best overall response to therapy.
- ORR (Overall Response Rate) is defined as the proportion of patients who have a partial or complete response as the best overall response to therapy.



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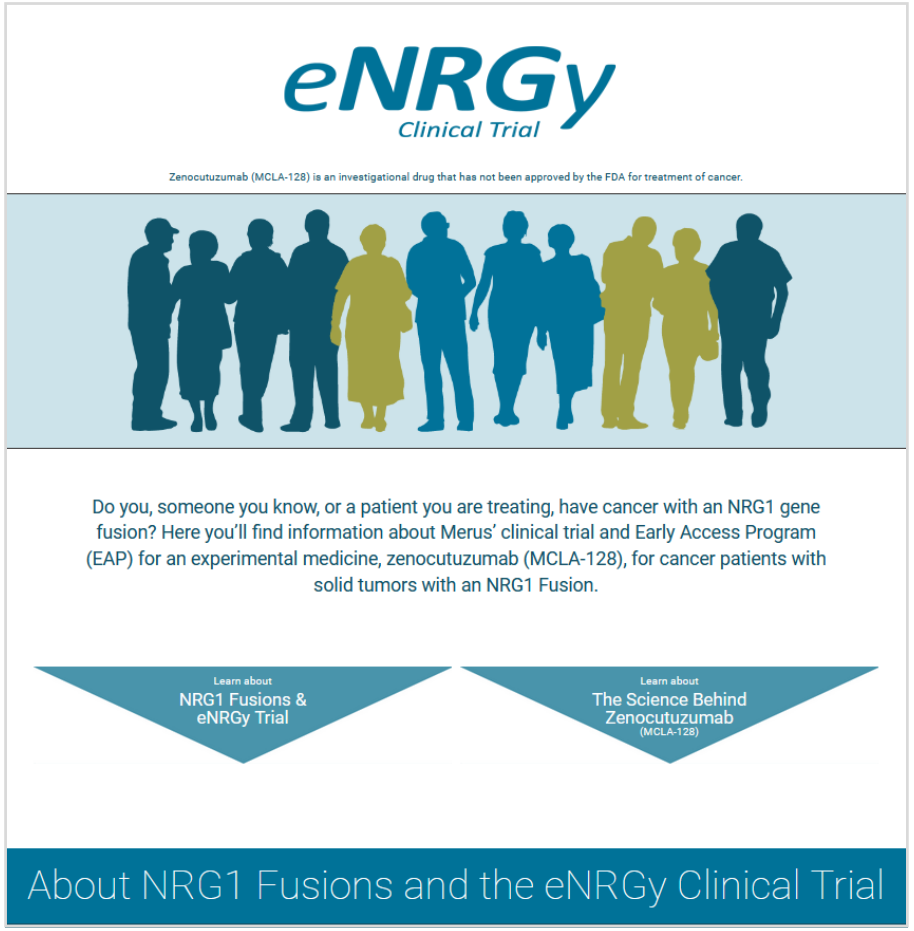
# MCLA-128 summary

- Demonstrated early clinical proof of concept in pancreatic and lung cancer patients harboring NRG1 Fusions
- Very well tolerated safety profile
- Unique ‘Dock and Block®’ mechanism of action and enhanced ADCC to inhibit the neuregulin/HER3 pathway in solid tumors harboring NRG1 Fusions
- Going forward, Merus will focus MCLA-128 program in Phase 1/2 eNRGy trial for patients with cancer harboring NRG1 Fusions

*Visit nrg1.com for more information*



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# Merus Approach to Bispecific Antibodies - Biclonics®



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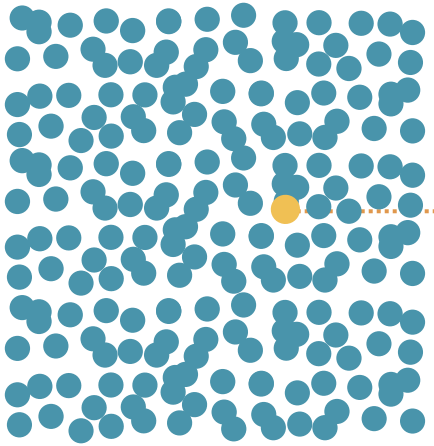
# Biclonics® are selected for differentiated activity in functional assays

## HUMAN ANTIBODY GENERATION

**MeMo®**
**Transgenic Mouse**

We use a proprietary transgenic mouse to generate panels of high-quality human antibodies

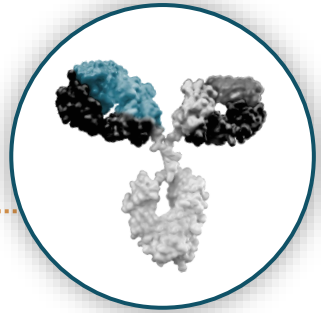
## BICLONICS® PANEL GENERATION



We can create up to 1,000 Biclonics® against any target pair of choice

lead identification

## FUNCTIONAL SCREENING



We use large-scale functional screening in cell-based assays to identify Biclonics® with novel modes of action



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# Merus Pipeline and Upcoming Milestones – 2020 and beyond



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# Merus clinical pipeline, near term milestones and program status

| PROGRAM | TARGETS | INDICATION / DRUG COMBINATION | PRE-IND | PHASE 1 | PHASE 2 | MILESTONE/STATUS |
|---|---|---|---|---|---|---|
| **MCLA-128** | HER3 x HER2 | NRG1 Solid tumors (monotherapy) | | | | Next update expected around end of 2020 |
| | | Metastatic Breast (combination in 2 cohorts) | | | | Phase 2 Results in 2020 |
| **MCLA-117** | CLEC12A x CD3 | Acute Myeloid Leukemia (AML) | | | | Initial Data 1H 2020 |
| **MCLA-158** | Lgr5 x EGFR | Solid tumors | | | | Trial Update YE 2019 |
| **MCLA-145** | CD137 x PD-L1 | Solid tumors Incyte (ex- U.S.) | | | | Dose Escalation Ongoing |
| **MCLA-129** | EGFR x c-MET | Solid tumors BETTA PHARMACEUTICALS (China) | | | | IND Enabling Studies Ongoing |
| **ONO-4685** | PD-1 x CD3 | Autoimmune disease ONO | | | | Phase 1 Trial Ongoing |
| **....** | Undisclosed | Autoimmune disease ONO | | | | |



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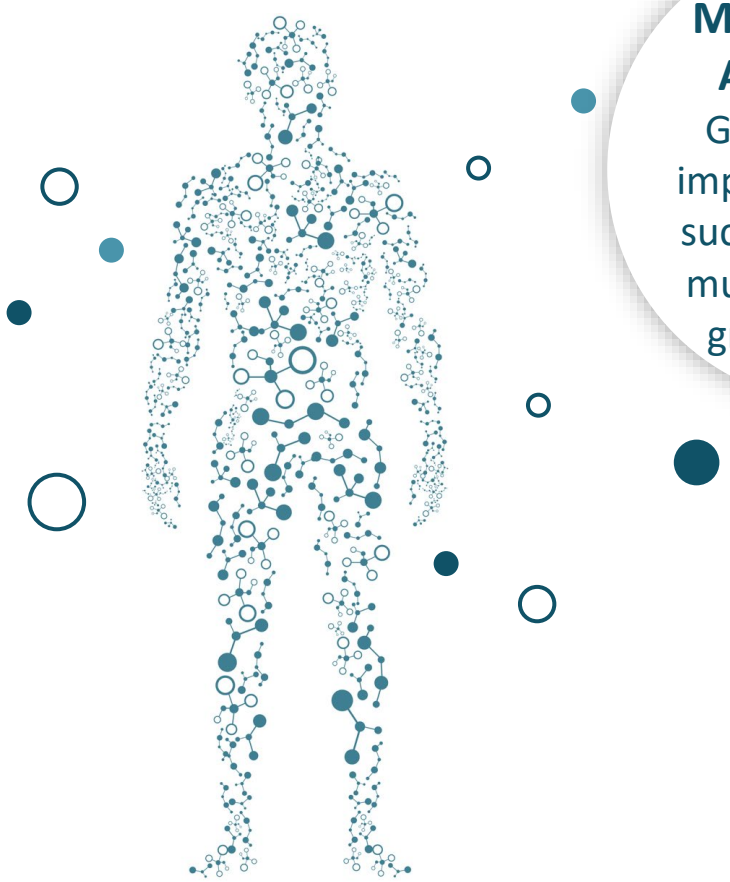
# Merus Biclonics®
# The next wave of antibody-based therapeutics in cancer treatment



**MONOCLONAL ANTIBODIES**
Game-changing impact, but limited success combining multiple mAbs for greater efficacy

**BISPECIFIC ANTIBODIES**
Offering novel modes of action and new biology

**KILL Cancer Cells**
with bispecific antibodies with novel modes of action

**BLOCK Immune Suppression**
in the tumor to strengthen immune activation

**ENGAGE T Cells**
to kill cancer cells and establish long-lasting anti-tumor responses

**HIGH POTENTIAL**
for Immunotherapy and Precision Medicine



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