Corporate Presentation

December 2014

Angiochem Highlights

- **Multi-faceted platform:**
  - **Peptide-Drug Conjugates** targeting LRP-1 receptor:
    - To cross the BBB and reach therapeutic concentrations in the brain
    - New Chemical Entities (NCEs) with new patent protection
  - **Proprietary 'Angiopep' peptides** linked to target drugs:
    - Small molecules, Proteins, Enzymes and Antibodies
- **Validated pipeline:**
  - *ANG1005*: peptide-paclitaxel conjugate
    - Clear antitumor activity in multiple tumor types (n≈200 patients)
  - ANG4043 and ADC: peptide-mAb and peptide-ADC conjugates
    - Clear efficacy in pre-clinical models
- **Key discovery collaborations**
  - GSK

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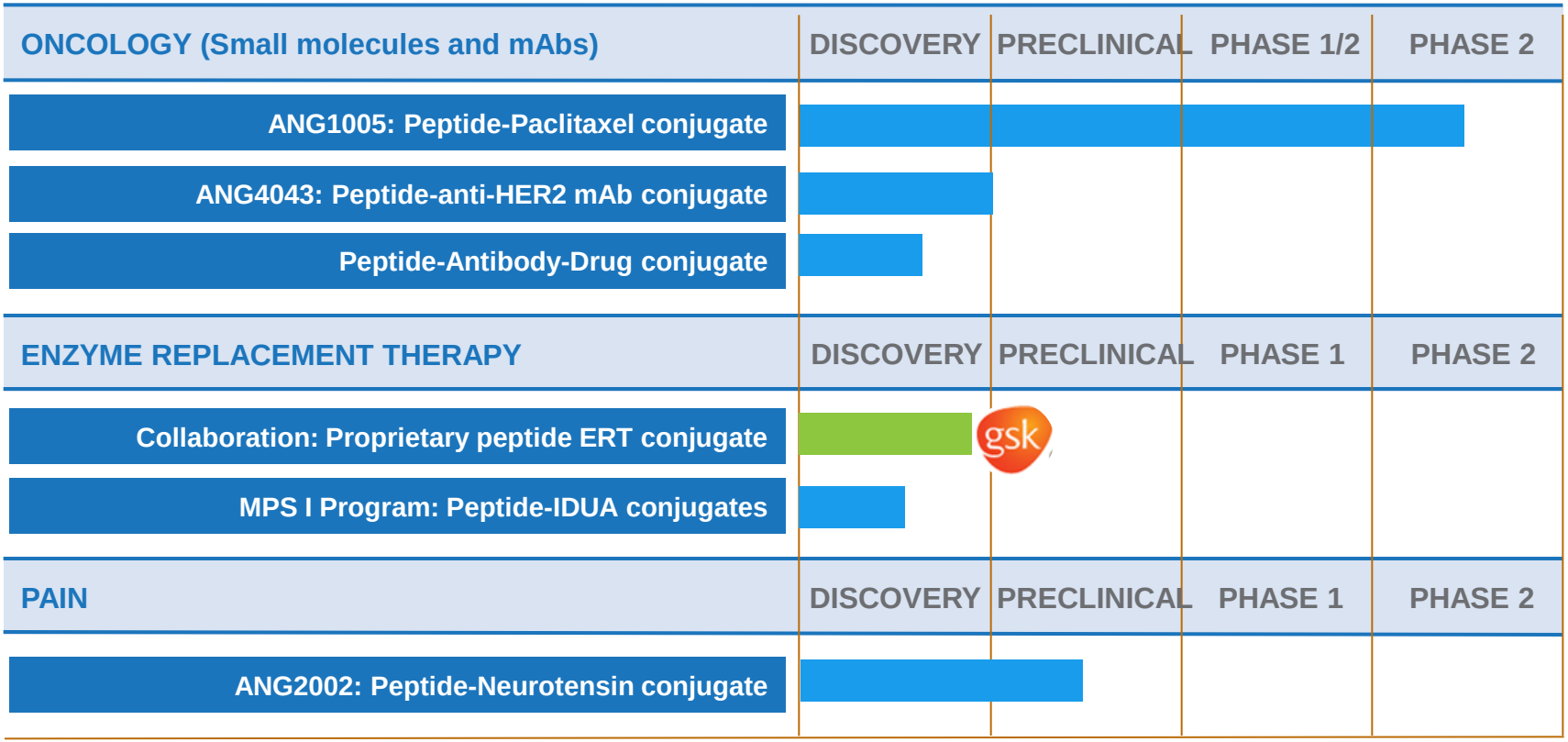
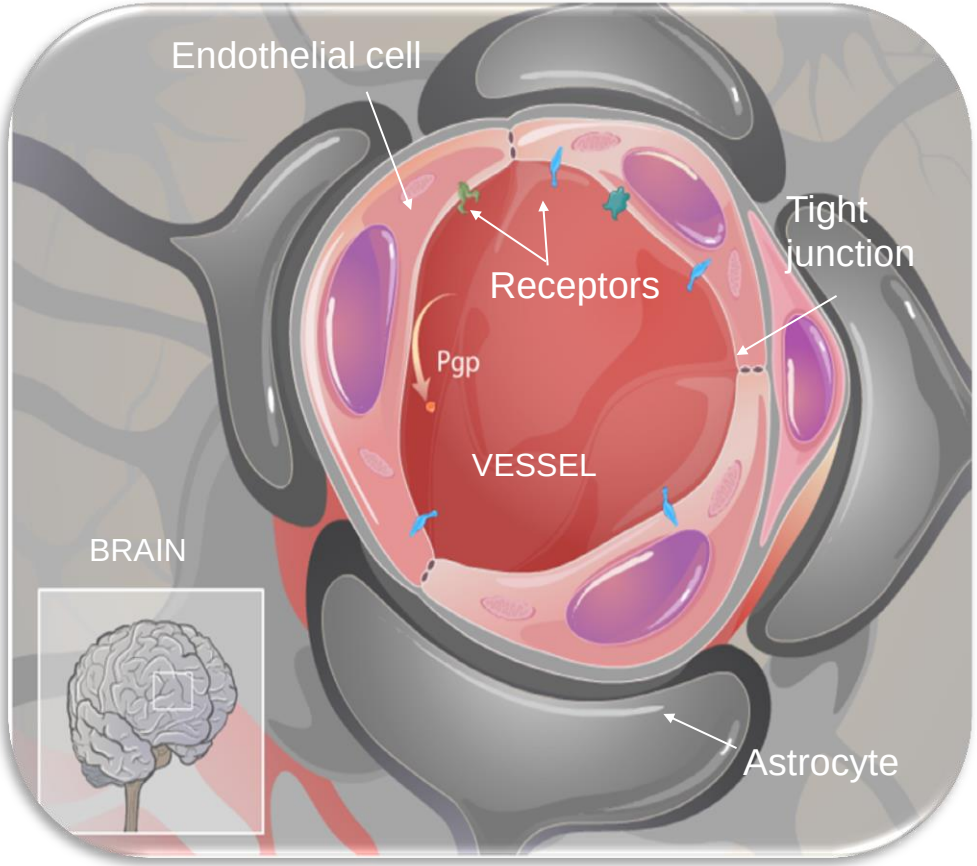
PIPELINE



The Blood-Brain Barrier

- Functions
  - Protects the Brain
    Tight junctions and Pgp activity prevent almost all foreign molecules
    penetrating the brain, preventing damage
  - Regulates Brain Homeostasis
    Receptors actively transport essential molecules into the brain, including glucose, insulin, growth hormones



>95% of drugs cannot penetrate the brain

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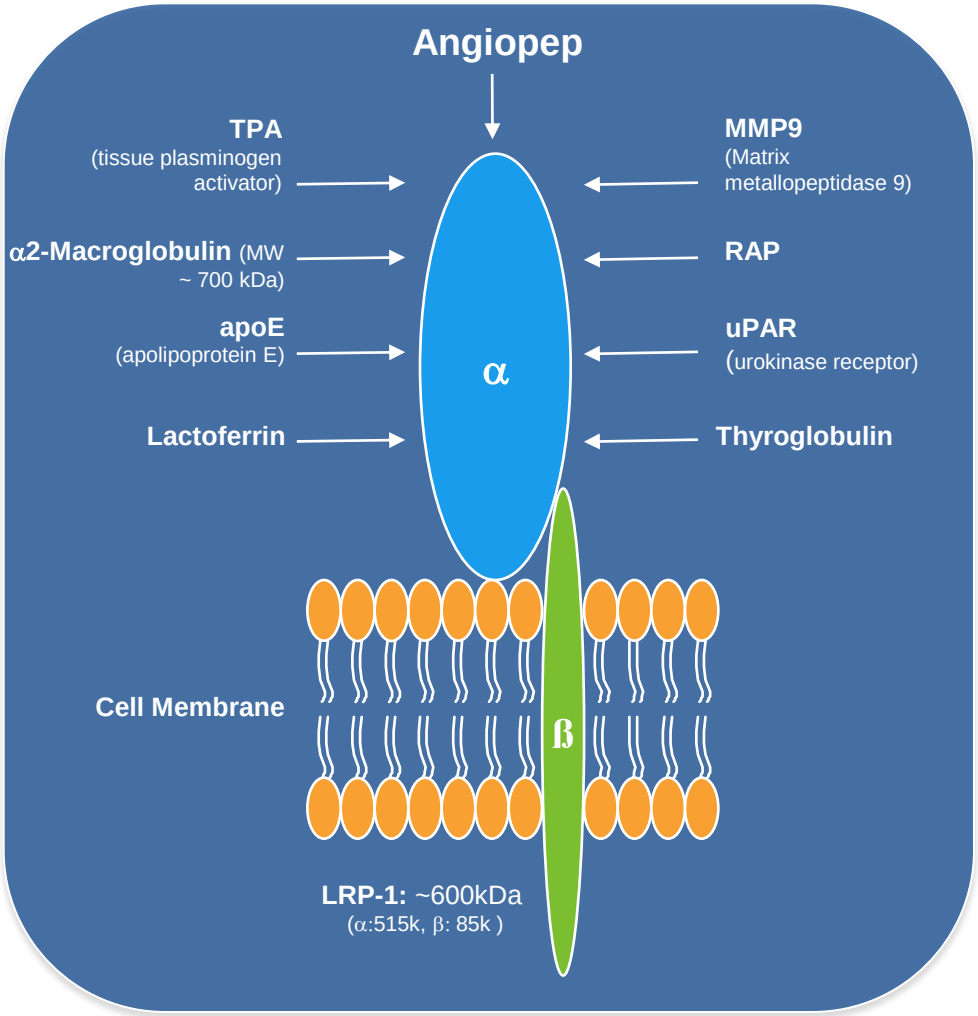
Angiochem Strategy: LRP1 receptor Targeting

- Angiopeps target LRP1 (Low density lipoprotein-related protein1), which is expressed on endothelial cells including those of the blood-brain barrier (BBB)
- LRP1 has over 40 known ligands, and one of its functions is receptor-mediated transcytosis of ligands across the BBB.



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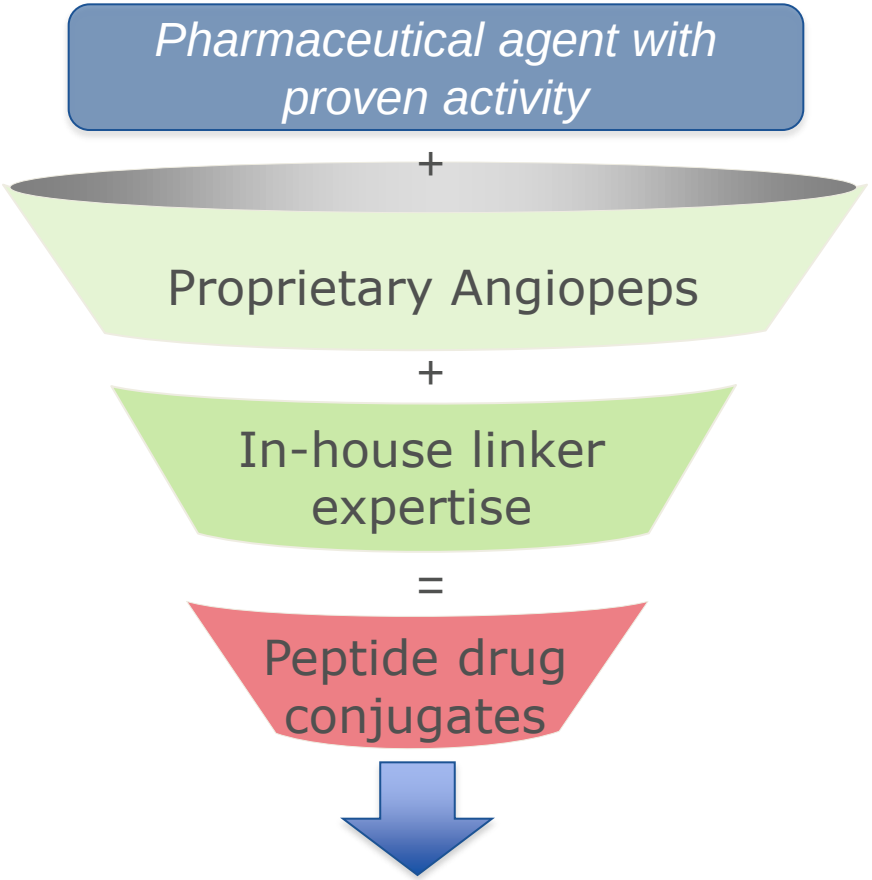
Angiopeps conjugated to therapeutics create novel brain-penetrant drugs

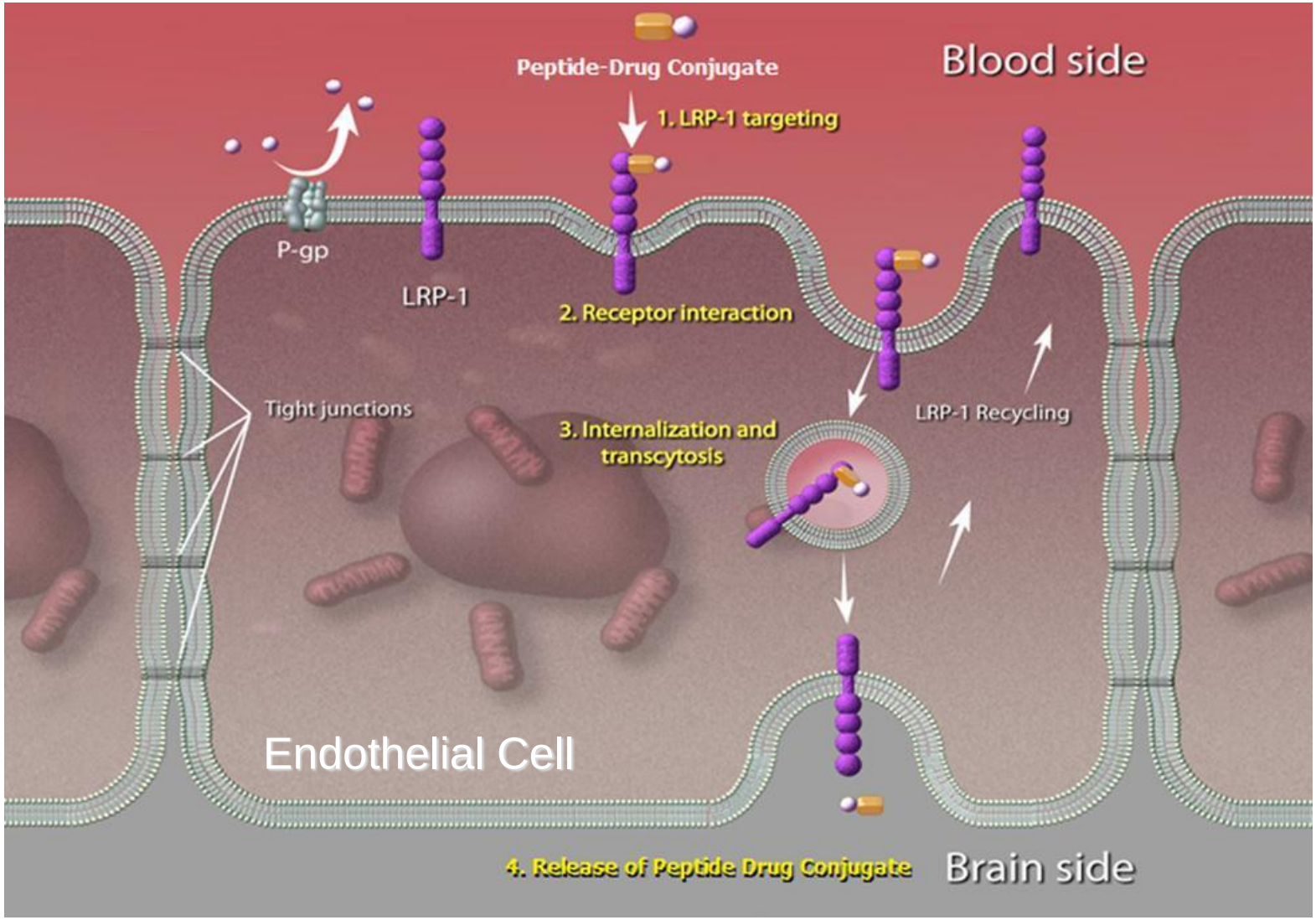


New Chemical Entities (NCEs):

•*Retain intrinsic pharmacologic activity*

plus *increased cell entry and transport across the BBB*

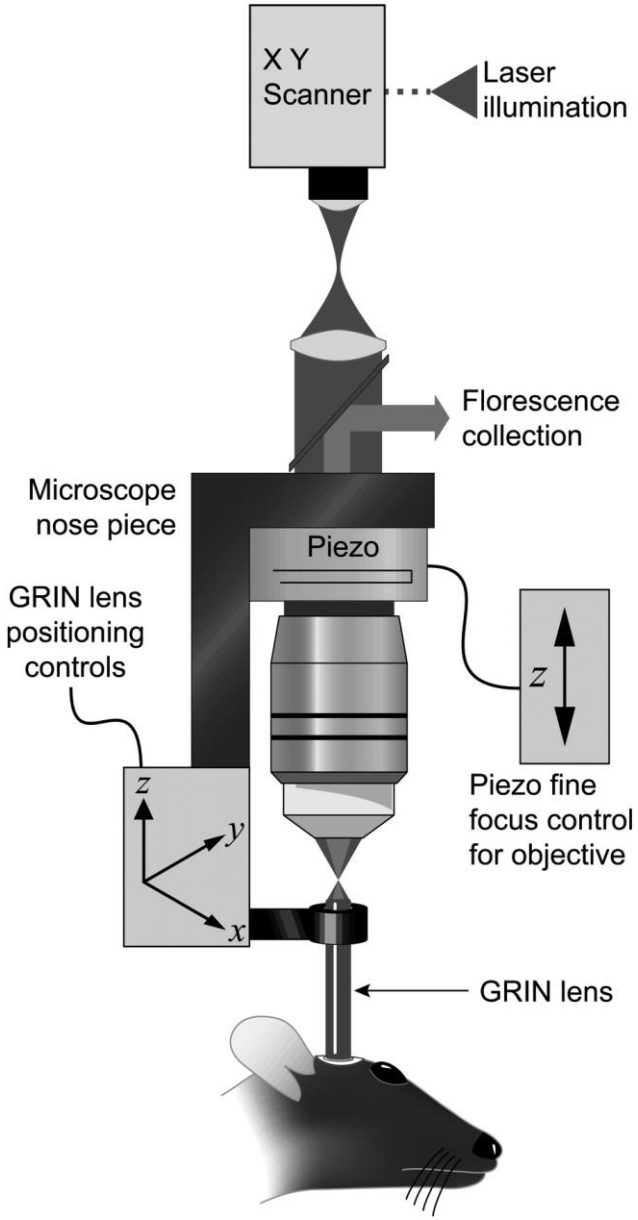
Crossing the BBB:
Receptor-Mediated Transcytosis Mechanism



Intravital analysis of Angiopep brain penetration in mice using two-photon microscopy

Procedure for real-time in vivo imaging:

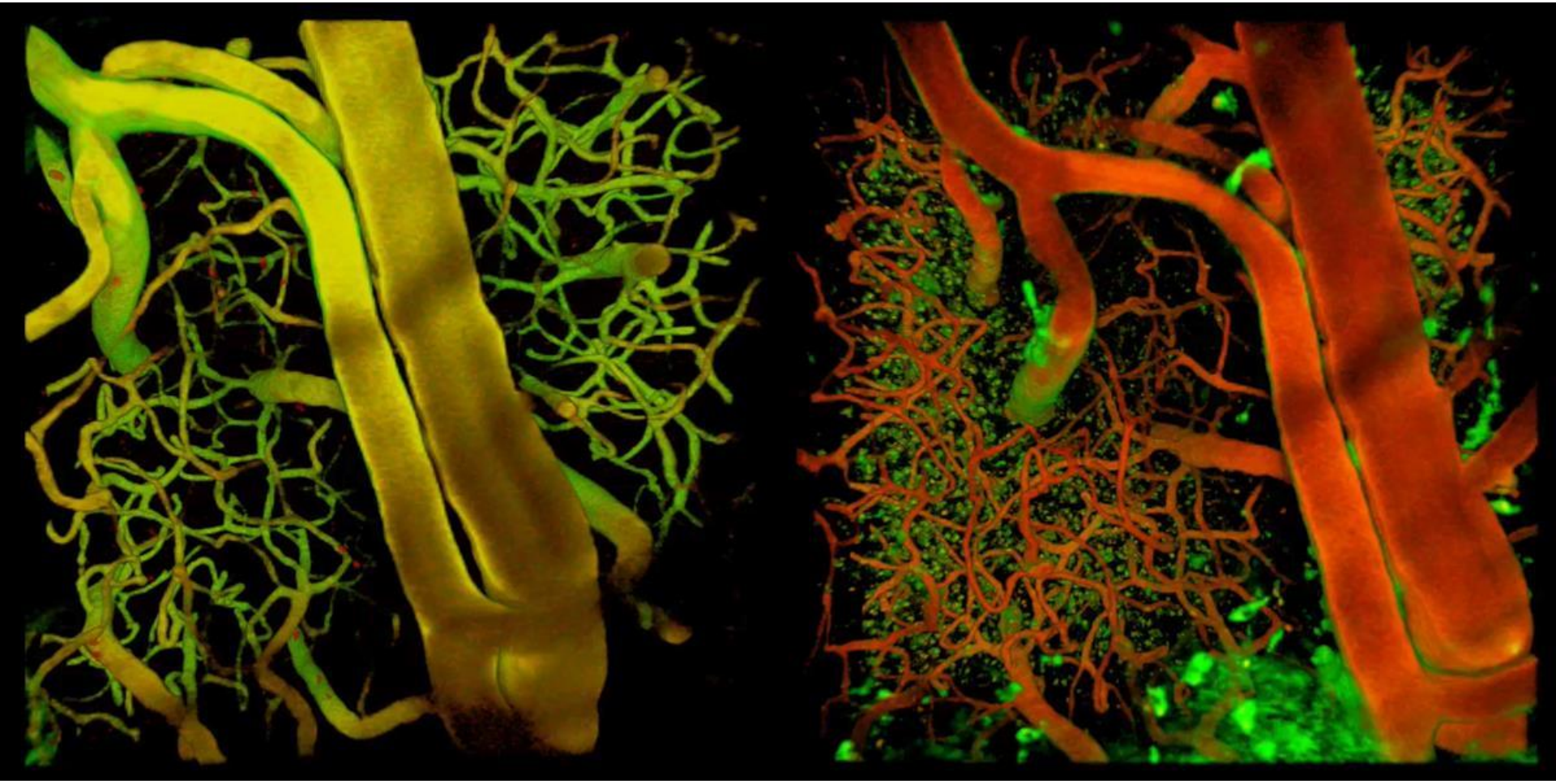
- Cranial window is installed; a 5mm round glass coverslip is laid on the dura mater
- Mice are allowed to recover during at least 3 weeks before intravital imaging experiments are initiated.
- Cy5.5-labeled Angiopeps are injected via tail vein.
- Immediately before imaging, Dextran Texas red is injected via the tail vein to label blood vessels.
- Intravital imaging is carried with an Olympus FV1000 multiple-photon excitation (MPE) two-photon microscope equipped with a Mai Tai DeepSee laser tuned at 890 or 905 nm and an Olympus Ultra 253 MPE water immersion objective (1.05 NA).
- Imaging depth 280 um



Angiopep brain imaging in 3D after IV injection

0 hrs

24 hrs



The image demonstrates, in a living mouse brain, that a conjugate (labelled with a fluorescent green probe Cy5.5) actively crosses the BBB into the brain parenchyma from the blood vessels (labeled with a circulating red dye- Dextran Texas Red).

ANG1005
Brain-penetrant paclitaxel
Clinical validation of LRP1 strategy

ANG1005 Phase I Clinical Program:Two Studies

Progressive Brain Metastases: Tumors of various primary origin

Efficacy in high dose group including MTD: (n=21)
- 5 Partial Response
- 71% disease control

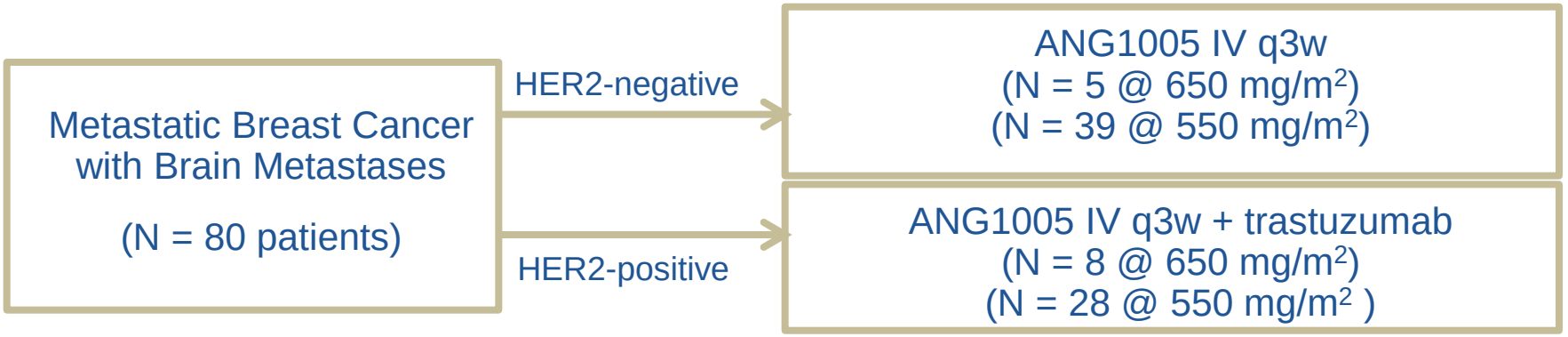
Recurrent Glioma

Efficacy in high dose group including MTD (n=28)
- 2 Complete Response and 2 Partial Response
- 61% disease control

Key Findings from both studies (119 total patients dosed in Ph I)

- Tolerability profile similar to Taxol
- No toxicity related to Angiopep-2
- No evidence of CNS toxicity as measured by neurocognitive testing and neurological exams
- No antibody production, even after repeat dosing to 22 cycles

Phase 2a study in HER2 +/- breast cancer patients with brain metastases



- Multi-center, open-label, single arm study with two cohorts (HER2-positive and HER2-negative).
- Adult patients with measurable (≥1 cm) brain metastases from breast cancer with or without prior WBRT and KPS ≥70.

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Best Intracranial Response Investigators' Measurements (ITT)

Phase II HER2+/- breast cancer patients with brain metastases, CP1005B016

Outcome by CNS RECIST	550 mg/m^2 HER2- (n=39)	550 mg/m^2 HER2+ (n=28)	650 mg/m^2 HER2- (n=5)	650 mg/m^2 HER2+ (n=8)
PR	5 (12.8%)	6 (21.4%)	0	4 (50%)
SD	14 (35.9%)	16 (57.1%)	3 (60%)	1 (12.5%)
PD	9 (23.1%)	1 (3.6%)	0	2 (25%)
Missing*	11 (28.2%)	5 (17.9%)	2 (40%)	1 (12.5%)
PFS rate at 3 mos	35.0%	71.3%	75.0%	71.4%
Median PFS	84 days	128 days	240 days	171 days
OS rate at 6 mos	59.6%	81.8%	75.0%	85.7%

***** Patients with tumor assessments less than 5 weeks from 1st treatment, or no post-baseline scans

Note: EDC data analysis April 9, 2014

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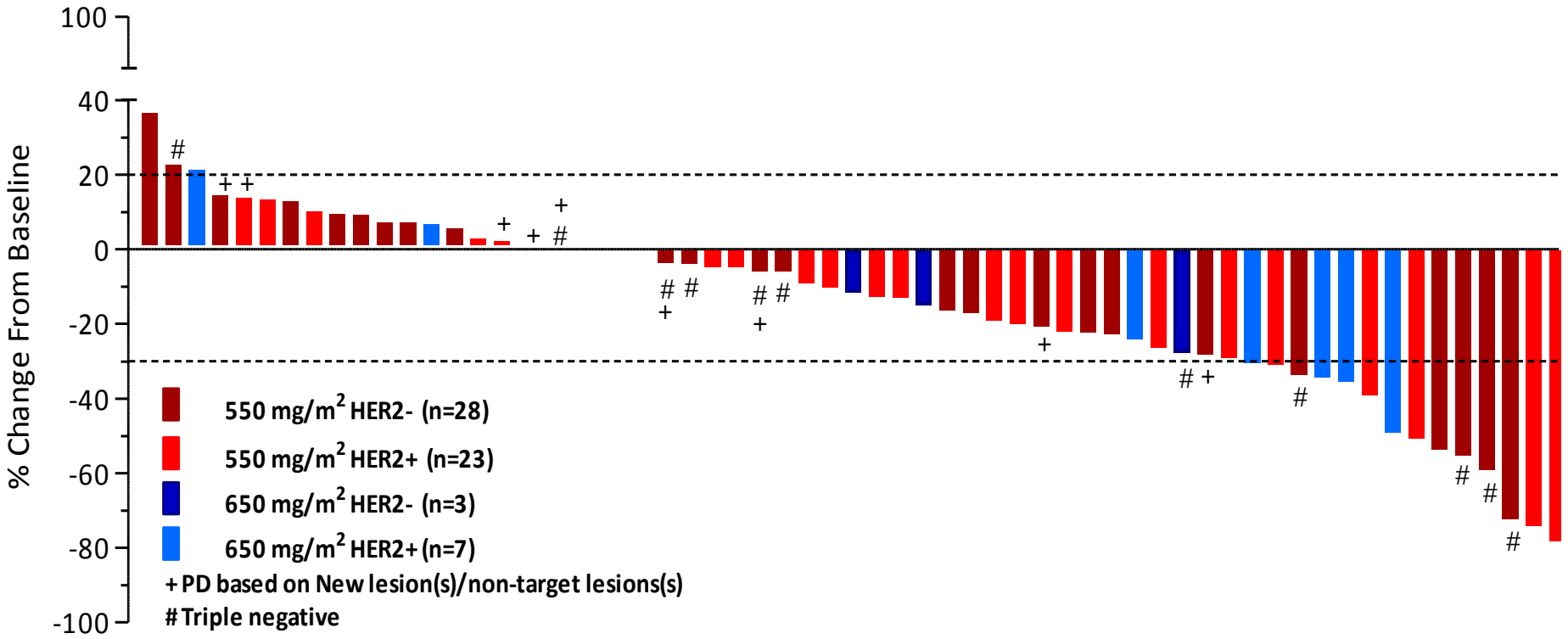
Best intracranial tumor responses:

Phase II HER2+/- breast cancer patients with brain metastases, CP1005B016



Data from patients who completed at least 1 post-treatment assessment at ≥ 5 weeks from 1st ANG1005 treatment; assessed by investigator per CNS RECIST v1.1.

Note: Data analysis May 12, 2014

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Case Study #1

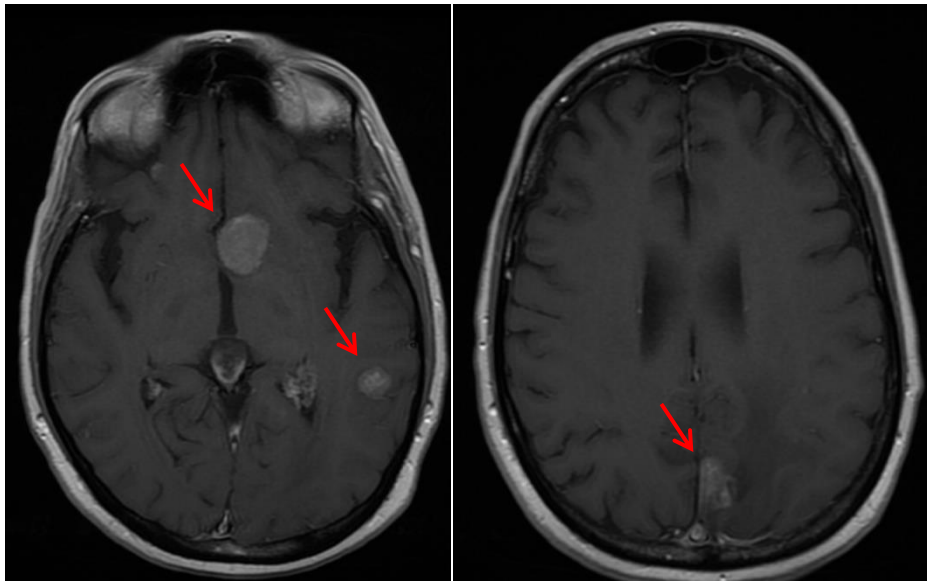
42-year old female

Dx: HER2+ breast cancer (Feb/09) relapsed with brain mets (Jul/09)

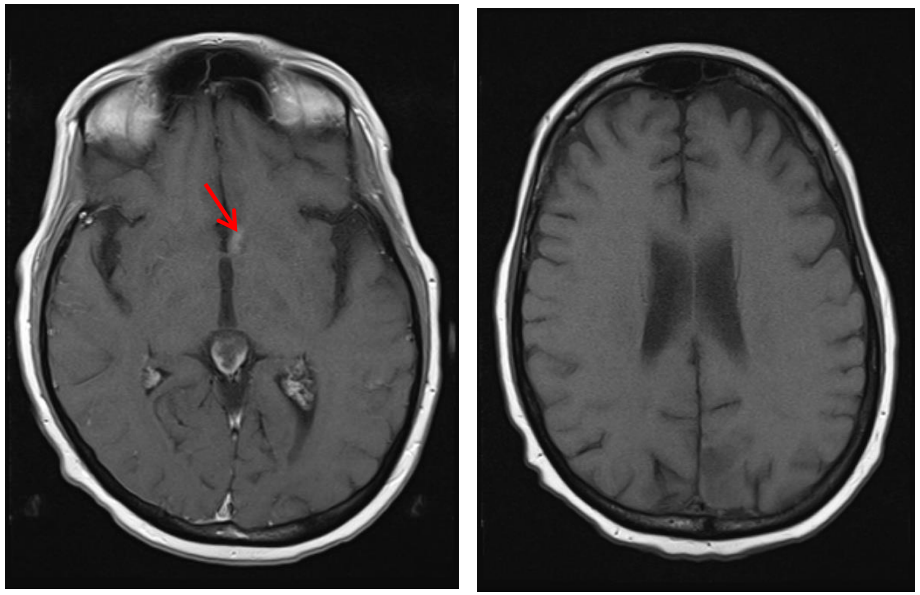
Prior Tx: SRS, neratinib, Herceptin/Tykerb, Xeloda/Tykerb, SRS, Herceptin/Tykerb, WBRT, Herceptin/Avastin, Taxol/carbo/Herceptin/Avastin

ANG1005: 15 cycles at 550mg/m^2

Partial responses up to 32 weeks



Baseline
29-Oct-2012
3 lesions: left caudate, left temporal lobe & left subinsaler cortex
T1 Axial Post



79%↓ in tumor size
24-Apr-2013 (Wk 24)
After 8 cycles of ANG1005
Out of the 3 lesions, only 1 lesion seen (left caudate)
T1 Axial Post

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Sub-Study Status at NCI

- Aim of the study is to evaluate the tumor response assess by MRI vs. FLT-PET
- 8 of 10 patients to date.
- First 7 patients have demonstrated brain tumor shrinkages by MRI and/or PET

Patient	# Cycles Received	Best MRI Response	% FLT-PET/CT Decrease (SUV_{max}) (week 3)
1	2	-5%	-44%
2	6	-32%	Tumors not seen
3	8	-14%	-29%
4	6	-18%	-38%
5	6	-60%	-67%
6	3	-15%	Not evaluated
7	12	-56% (8 months)	-50%
8	1	-	-

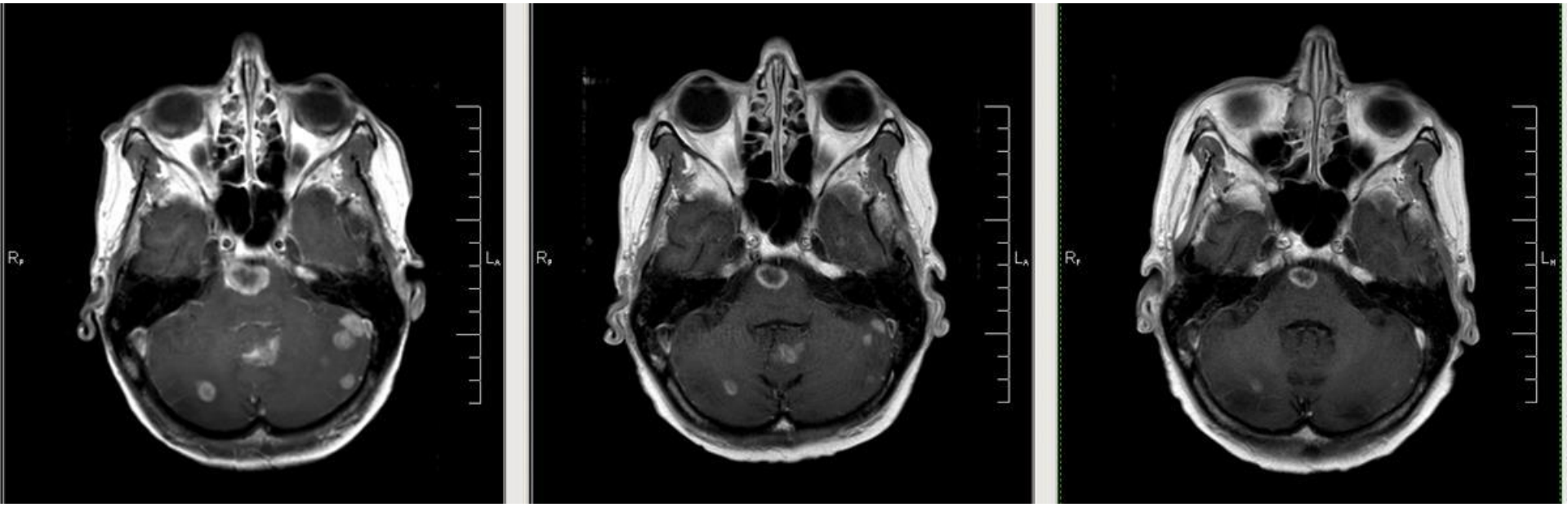
Case Study #2

NCI #7: 56-year old female

Dx: HER2+ breast cancer (1997) relapsed with brain mets (Nov 2011)

Prior Tx: Sx, Adrimycin/Cyclophosphamide, Tamoxifen, Taxol/Capecitabine, Taxol/Carboplatin/Herceptin, Herceptin, Lapatinib/Herceptin, Capecitabine, Lapatinib/Capecitabine, WBRT

Main symptoms at baseline: gait disturbance and headache – ***both improved after 1st ANG1005 treatment and patient continues to do well***



Baseline

After 2 Cycles
Week 6
32% decrease

After 4 Cycles
Week 12
43% decrease

Abstract: Evaluation of CNS and peripheral anti-tumor activity of ANG1005 in patients with brain metastases from breast tumors and other advanced solid tumors

Poster Highlights Session: Developmental Therapeutics: Clinical Pharmacology and Experimental Therapeutics

Nancy U. Lin[1], Nashat Y. Gabrail[2], John Sarantopoulos[3], Lee Steven Schwartzberg[4], Santosh Kesari[5], Susan Elaine Bates[6], Carey K. Anders[7], Anthony D. Elias[8], Jean-Paul Castaigne[9], Vihra Iordanova[9], Betty Lawrence[9,] Razelle Kurzrock[5]

1Dana-Farber Cancer Institute, Boston, MA; 2Gabrail Cancer Center, Canton, OH; 3Institute for Drug Development, Cancer Therapy and Research Center, University of Texas Health Science Center San Antonio, San Antonio, TX; 4The West Clinic, Memphis, TN; 5University of California, San Diego, La Jolla, CA; 6Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD; 7The University of North Carolina at Chapel Hill, 8Lineberger Comprehensive Cancer Center, Chapel Hill, NC; University of Colorado Cancer Center, Aurora, CO; 9Angiochem, Inc., Montreal, QC; Angiochem Inc., Montreal, QC

Intracranial and peripheral anti-tumor activity of ANG1005 in Phase I and Phase II

Study	Ph I: Solid Tumors (ANG1005-CLN-02)		Ph II: Breast Cancer (CP1005B016)			
Dose Level	≥ 420 mg/m^2		550 mg/m^2		650 mg/m^2	
Best Response	Intracranial	Peripheral	Intracranial	Peripheral	Intracranial	Peripheral
Sample Size	N=18	N=16	N=51	N=28	N=10	N=4
CR	0	0	0	1 (4%)	0	0
PR	4 (22%)	4 (25%)	11 (22%)	7 (25%)	4 (40%)	1 (25%)
SD	10 (56%)	7 (44%)	30 (59%)	14 (50%)	4 (40%)	2 (50%)
PD	4 (22%)	5 (31%)	10 (20%)	6 (21%)	2 (20%)	1 (25%)

Peripheral tumor reductions observed in liver, lung, bone and lymph nodes

Phase I: From the patients dosed at ≥ 420 mg/m^2,18 were evaluated for intracranial, 16 for peripheral efficacy and 21 for overall response

Phase II: 61 evaluated for intracranial and 32 for peripheral efficacy

Note: Data analysis May 12, 2014

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ANG1005 On-going studies

- Sub-study at NCI in breast cancer with brain met to evaluate the tumor response assess by MRI vs. FLT-PET
  - https://clinicaltrials.gov/ct2/show/NCT01480583
- Phase 2a in recurrent glioma focusing on Grade III
  - https://clinicaltrials.gov/ct2/show/NCT01967810
- Phase 2b in breast cancer with brain metastasis
  - First patient enrolled in October 2014; already showing tumor shrinkage
  - https://clinicaltrials.gov/ct2/show/NCT02048059

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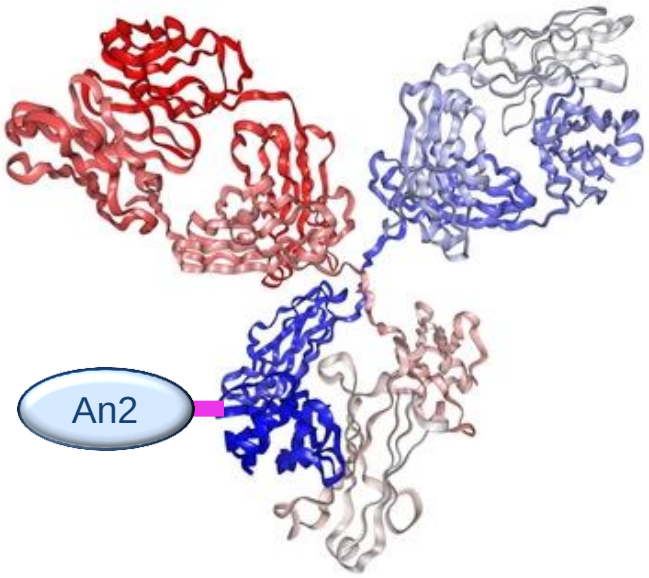
An2-mAb Conjugate ANG4043 and Brain-Penetrant ADCs

ANG4043, a brain-penetrant mAb for HER2-positive brain metastases



- ANG4043 is a chemical conjugate of the anti-HER2 mAb with Angiopep-2.
- This NCE is not a biosimilar (patents filed 2012)
- ANG4043 has potential to be a First-in-Class agent for HER2+ breast cancer brain metastases.

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Four Requirements for Brain Cancer Treatment

1. Must enter brain without harming or compromising the BBB (unlike mannitol or ultrasound)
2. Must have demonstrated efficacy against brain tumors
3. Must address peripheral tumors as well
4. Must not impact patient QOL or introduce additional AEs

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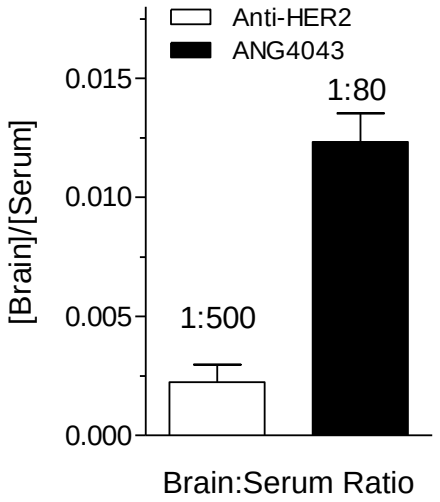
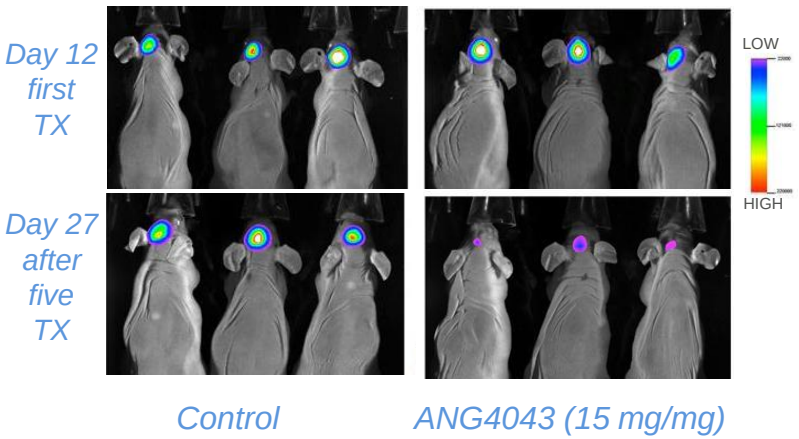
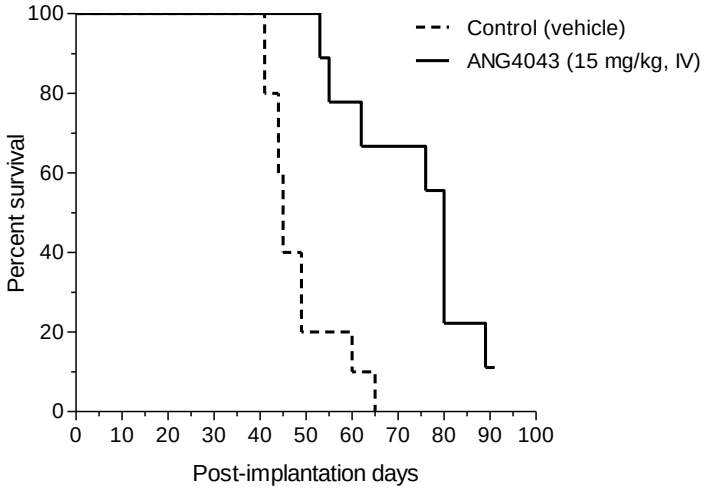
ANG4043 Meets Brain Cancer Treatment Criteria

1. Enters brain in a natural way, without compromising BBB ✓



2. Targets tumors, reduces tumor size, and increases survival in a mouse intracranial tumor model ✓



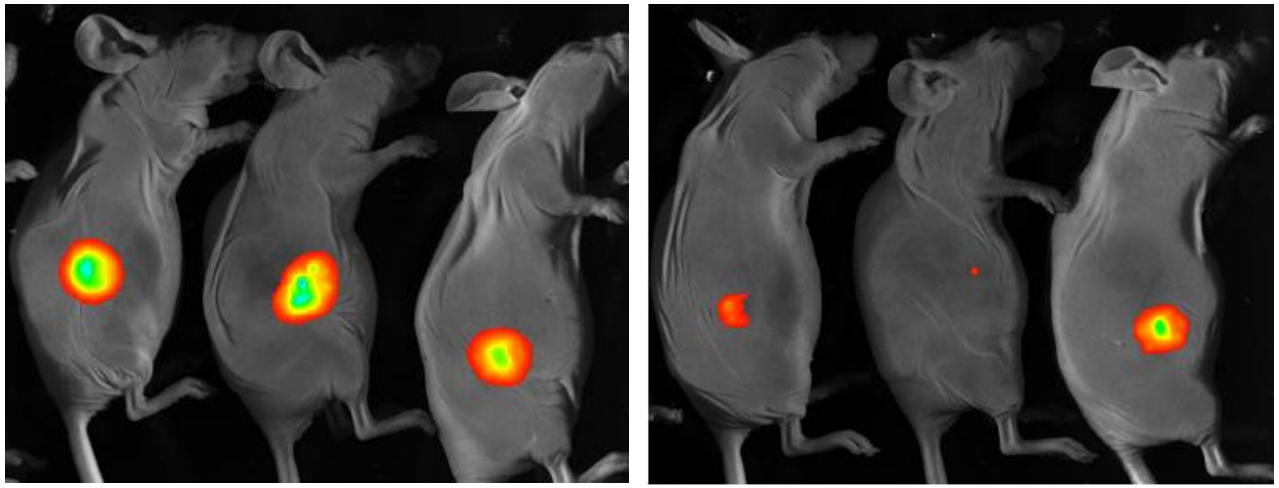


ANG4043 Meets Brain Cancer Treatment Criteria

Before

After a single treatment

37 days post-implantation; Mice received single IV dose, 15 mg/kg



7 days post-treatment

Anti-HER2 *ANG4043* *Vehicle*

Anti-HER2 *ANG4043* *Vehicle*

3. Effective against peripheral tumors ✓

4. Does not reduce QOL (well tolerated at highest dose tested, 50 mg/kg) ✓

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Publication

Large Molecule Therapeutics

Molecular Cancer Therapeutics

ANG4043, a Novel Brain-Penetrant Peptide–mAb Conjugate, Is Efficacious against HER2-Positive Intracranial Tumors in Mice

Anthony Regina[1], Michel Demeule[1], Sasmita Tripathy[2], Simon Lord-Dufour[1], Jean-Christophe Currie[1], Mustapha Iddir[3], Borhane Annabi[3], Jean-Paul Castaigne[1], and Jean E. Lachowicz[1]

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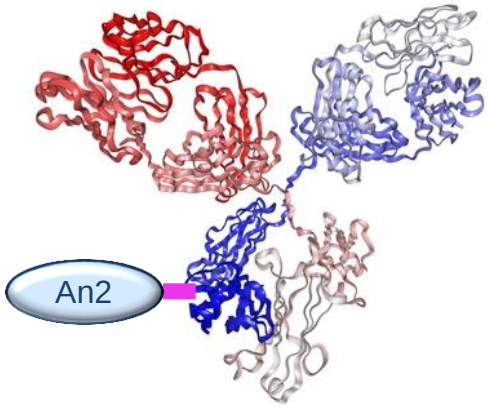
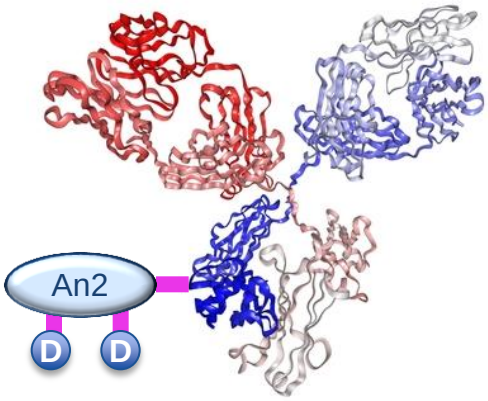
Angiochem ADC discovery research





POC for An2-mAb established with ANG4043

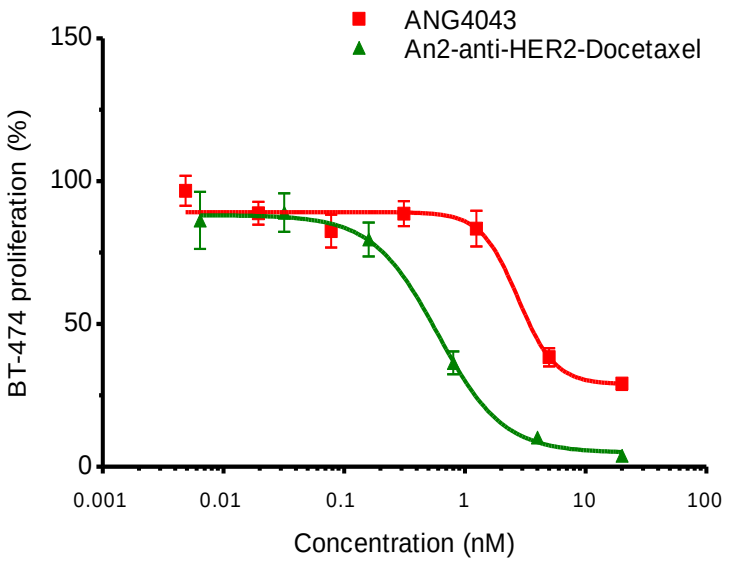
- Retains affinity for HER2 receptor and anti-proliferative activity
- Enters brain and targets HER2+ tumors
- Reduces tumor size and increases survival

mAb/oncology field has shifted attention to ADCs.

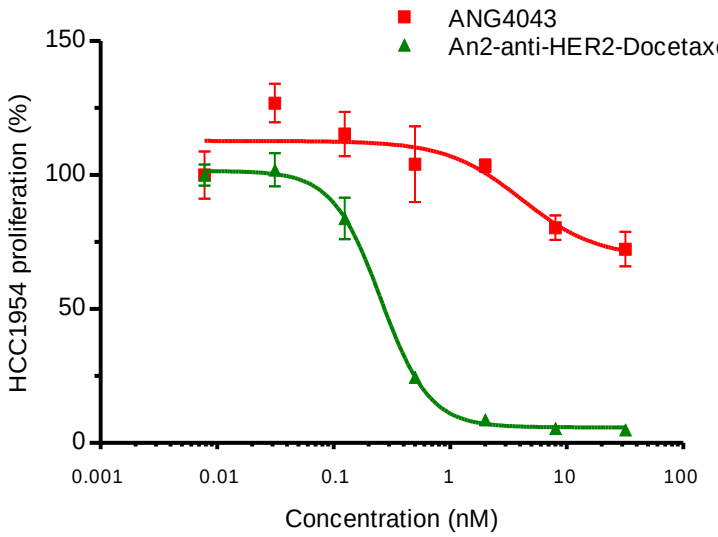
- Linker is recognized as the key to success for controlling release of drug from mAb.
- Angiochem's has deep expertise with peptide drug and peptide mAb linkers.
- Our linker experience is a natural fit for ADC discovery.

Potent anti-proliferative effect of ADCD1 on HER2+ breast cancer cells

BT-474 cells: sensitive to Trastuzumab



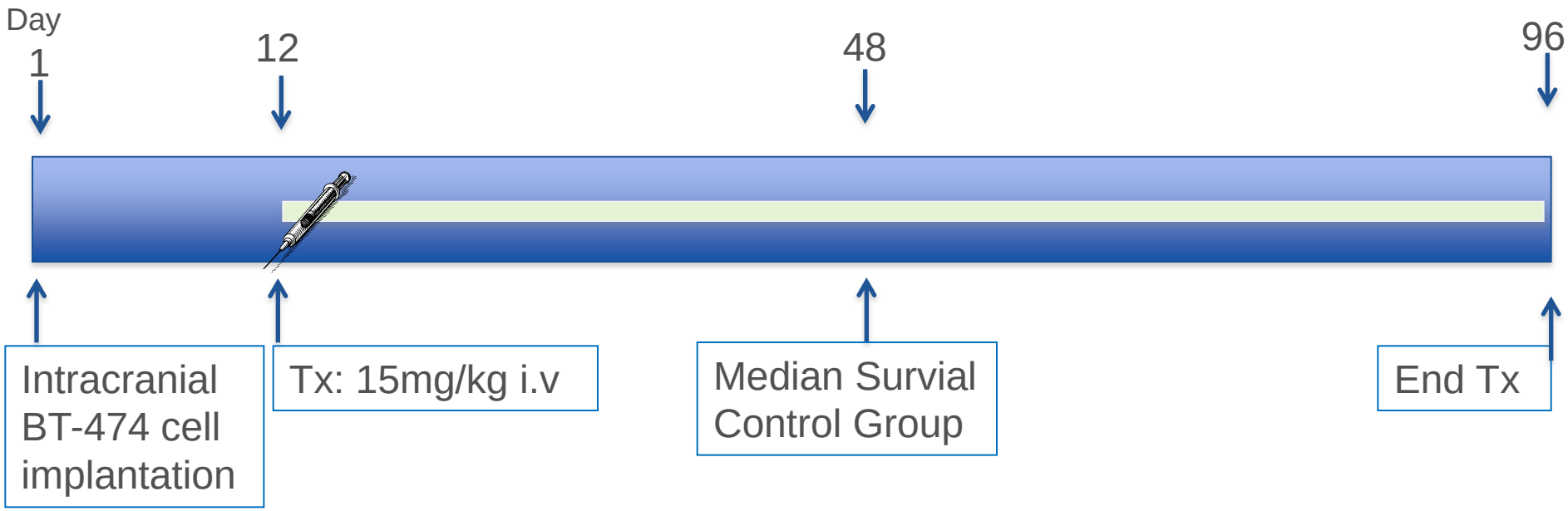
HCC-1954 cells: Resistant to Trastuzumab



Compilation of proliferation assay IC_{50} (nM)

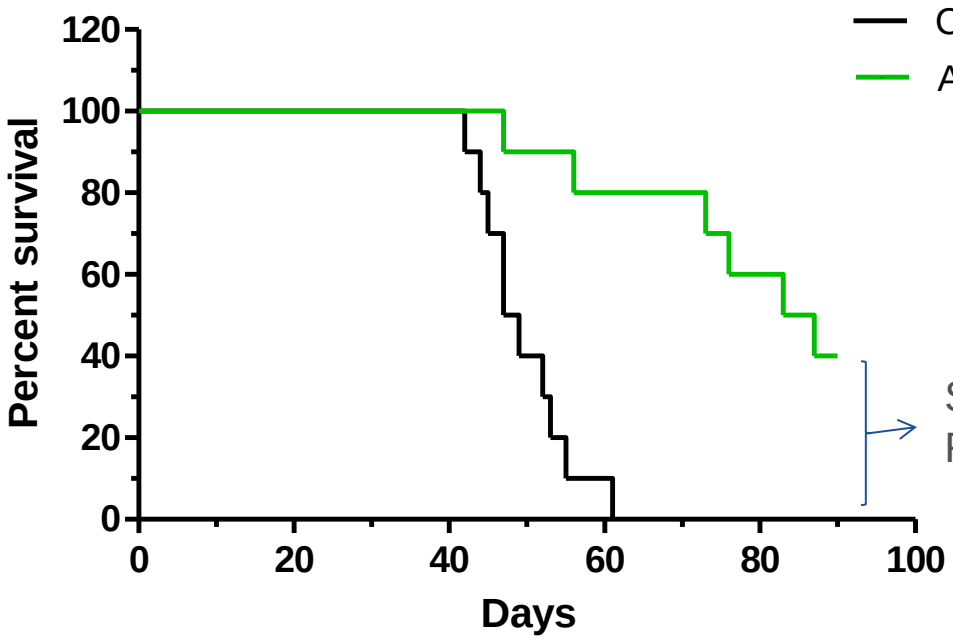
Compounds	Sensitive BT-474 cells	Resistant HCC-1954 cells
Anti-HER2	3.6 ± 1.6	---
ANG4043	3.7 ± 1.7	---
An2-anti-HER2-Docetaxel	0.6 ± 0.4	0.2 ± 0.1

Intracranial BT-474 tumor model: Comparison An2-ADC imaging/survival study



Treatments	Frequency
Control	Every two weeks
ADCD1	Twice weekly

ADCD1 improves survival in BT-474 intracranial tumor-bearing mice



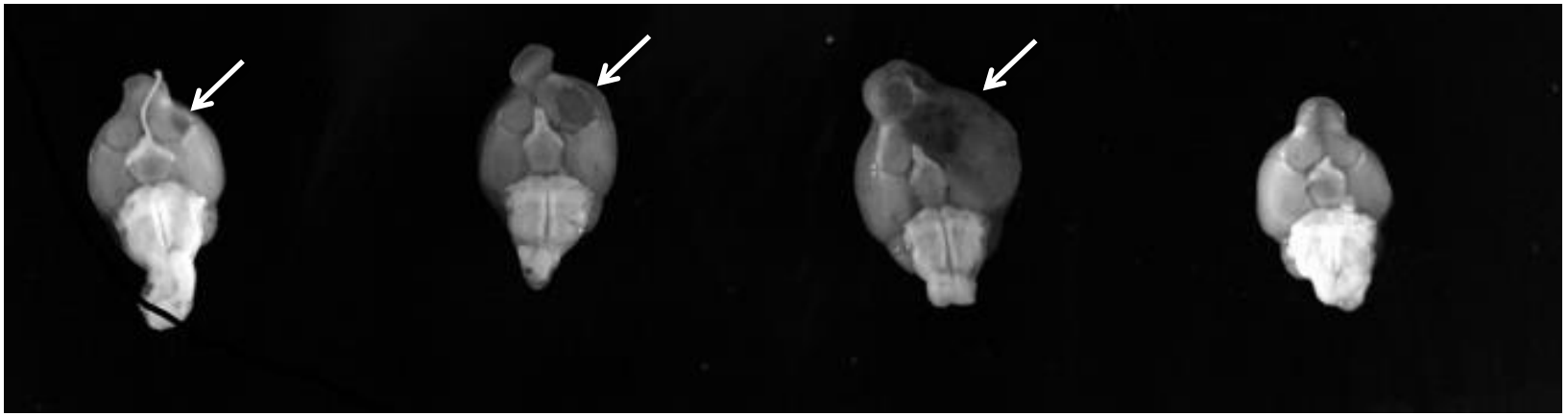
Study ended at 2x control survival.
Four mice remained living in ADCD1 group.

Treatment	Median survival (days post-implant)	Increase Post-treatment
Vehicle	48	
An2-anti-HER2-Docetaxel	87	+108%

P=0.0001

Tumors in ADCD1 mice sacrificed at end of study

- At day 96 (double the median of control group), 4 remaining animals were sacrificed
- One mouse had no visible tumor (right)
- One mouse had a large tumor (second from right)
- Two mice had small tumors (left two)



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ANG2002
for treatment of pain

Biological Rationale: Neurotensin

- Neurotensin is a tridecapeptide neurotransmitter found in spinal cord and brain (including periaquiductal grey, a major center for pain processing).
- Evidence for NT analgesia has accumulated since the 1980's.
- The analgesic activity of NT is elicited by excitation of neurons that activate descending inhibitory nerve fibers to dorsal horn neurons involved in the mediation of pain (Behbehani and Pert, 1984).
- Intrathecal or intracerebral ventricular administration is required for efficacy, as NT does not cross the BBB

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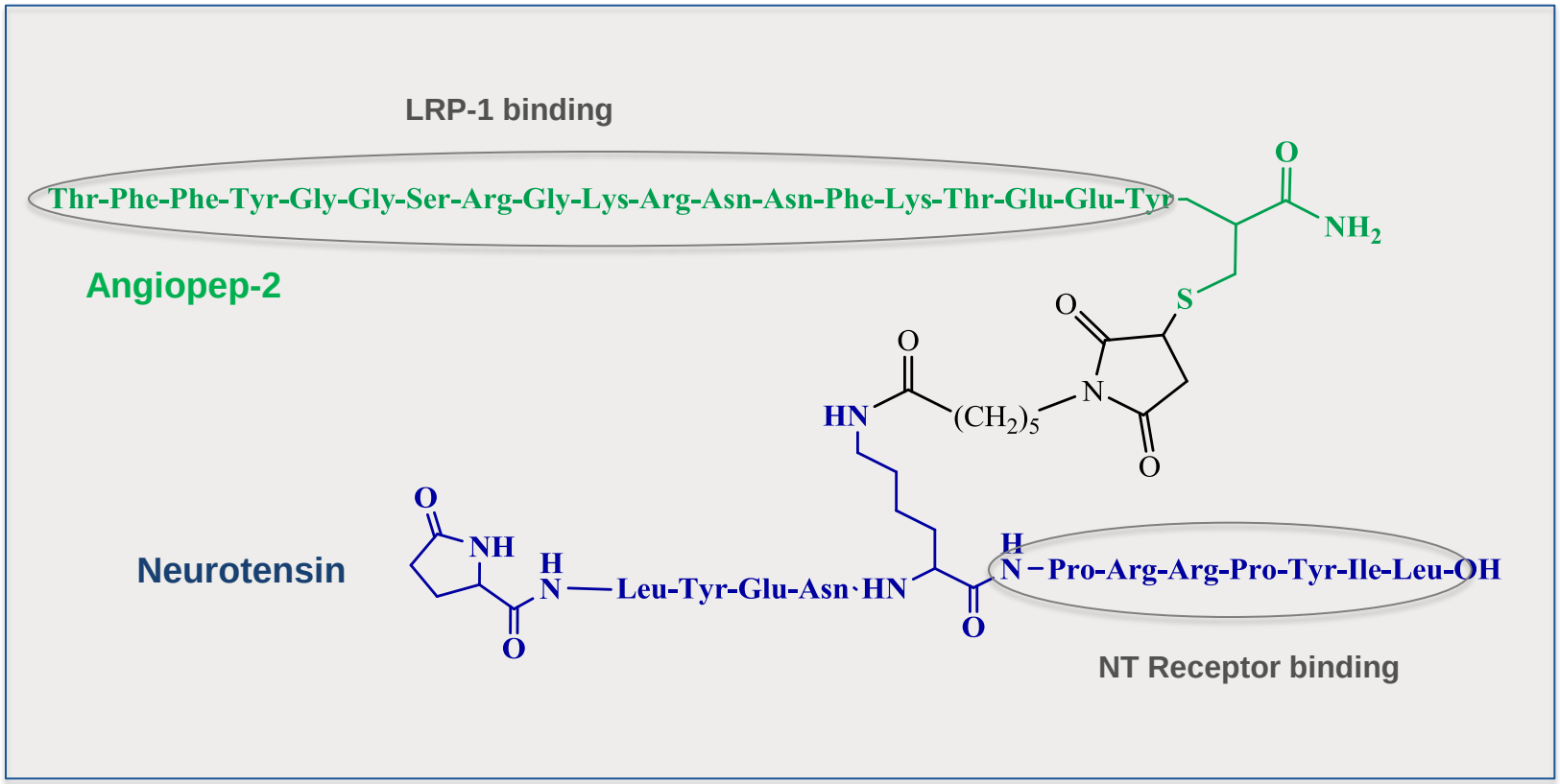
An2-Neurotensin: ANG2002



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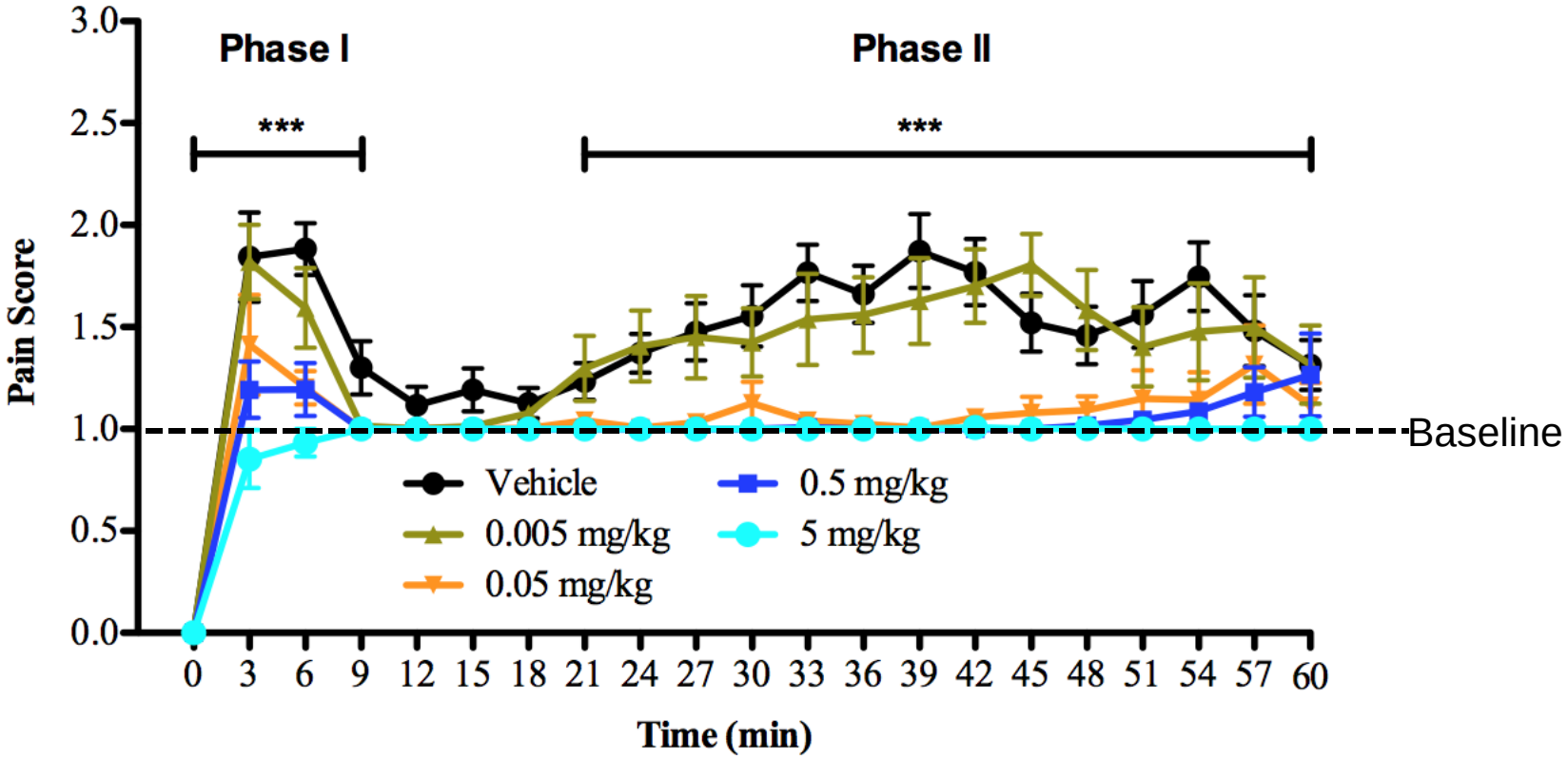
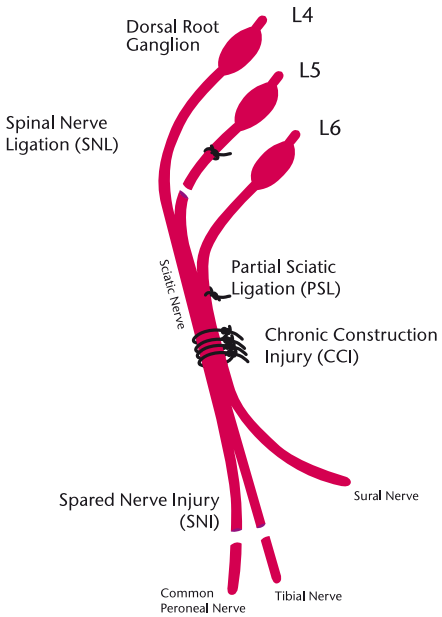
ANG2002 is effective in the rat formalin injection model of inflammatory pain

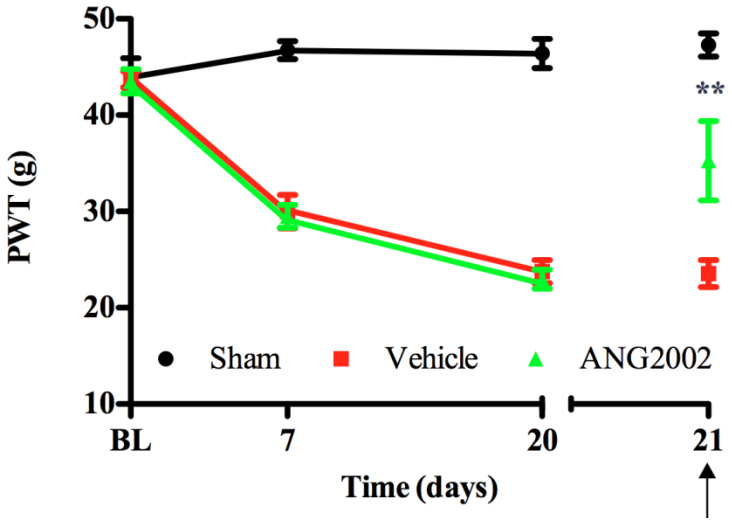


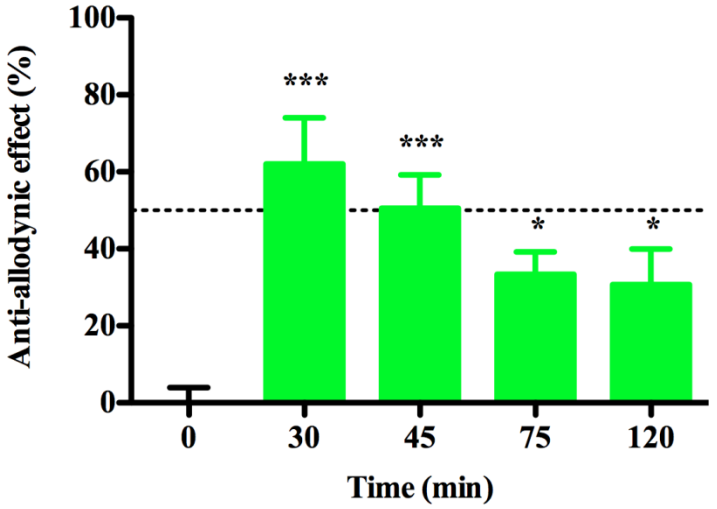
In this model, an intraplantar injection of the irritant formalin is given. Pain is scored by recording time spent in aversive behaviors such as flinching and biting or licking the injection site. The acute pain (Phase I) is followed by inflammatory pain (Phase II).

ANG2002 is effective in the rat chronic constriction injury neuropathic pain model



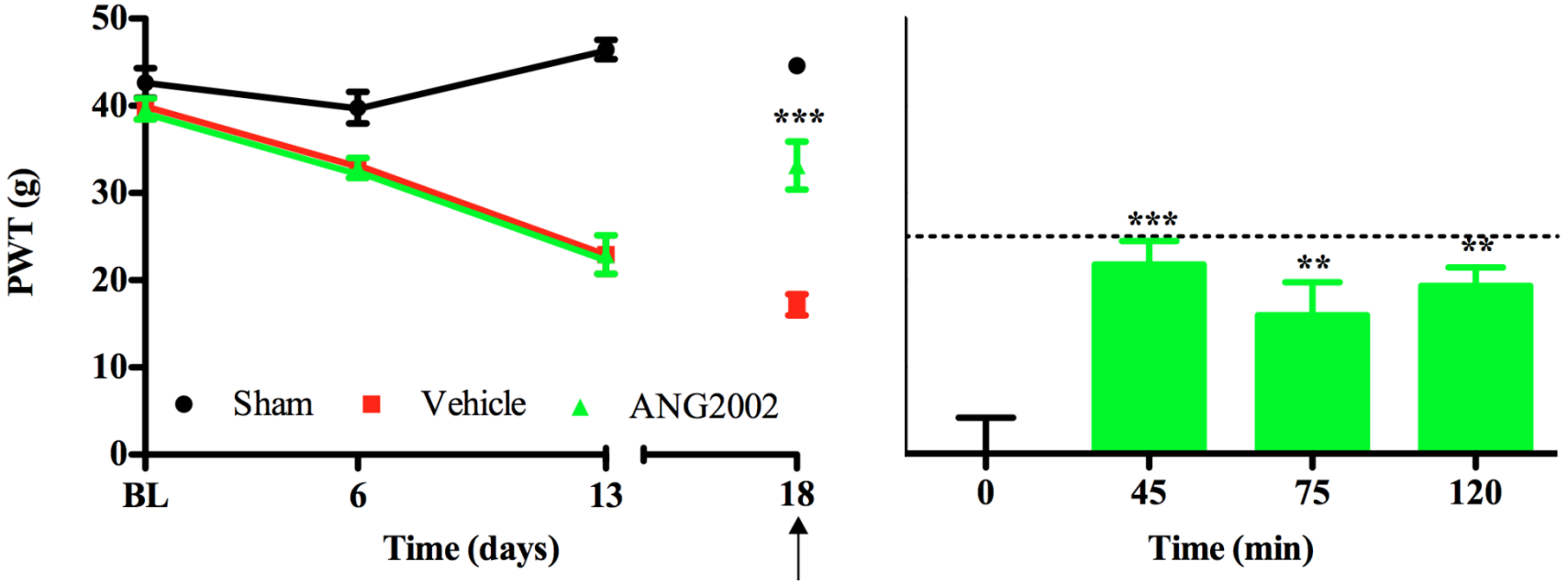
Model: The sciatic nerve is ligated to model a constriction injury. After 21 days, paw withdrawal threshold, PWT, is measured by testing the force of a Von Frey fiber that will induce paw withdrawal.





Treatment, 0.05 mg/kg, iv

ANG2002 (0.05 mg/kg) is effective in alleviating allodynia in rats with bone tumors



Treatment: 0.05 mg/kg, iv

ANG2002 Summary

- ANG2002 is a chemical conjugate of the 19-mer An2 peptided and the 13-mer full-length NT.
- ANG2002 retains affinity for NT receptors and potency for NT signaling in vitro.
- Unlike native neurotensin, ANG2002 is analgesic when delivered systemically.
- ANG2002 is effective in models of
  - Inflammatory Pain
  - Neuropathic Pain
  - Cancer Pain

Company Overview

- **Corporate Profile**
  - Founded in 2003, employ 25 FTEs in Montreal, Canada
- **Leadership Team**
  - **Jean-Paul Castaigne**, MD, MBA; President and CEO

    Experience in research and development, sales and marketing, IP, business development and company strategic management with Sanofi-Aventis, J&J, Novartis, Fournier and ConjuChem
  - **Michel Demeule,** Ph.D.; Director of Research

    Scientific co-founder, experience in BBB & cancer research
  - **Catherine Gagnon**, M.Sc; Director of Corporate Development

    Previously with ConjuChem
  - **Jean Lachowicz,** Ph.D., MBA; CSO

    Previously with Merck & Co and Schering-Plough
  - **Betty Lawrence;** VP of Development

    Previously with Health Canada, Resolution and ConjuChem

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Thank You

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