UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report: June 9, 2014
(*Date of earliest event reported*)

CELLECTAR BIOSCIENCES, INC.
(*Exact name of registrant as specified in its charter*)

Delaware	**333-119366**	**04-3321804**
(State or other jurisdiction of incorporation)	*(Commission File Number)*	*(IRS Employer Identification Number)*

3301 Agriculture Drive
Madison, WI 53716
(*Address of principal executive offices*)

(608) 441-8120
(*Registrant's telephone number, including area code*)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

ITEM 5.03 AMENDMENTS TO ARTICLES OF INCORPORATION OR BYLAWS

Effective at the close of business on June 13, 2014, we amended our second amended and restated certificate of incorporation to effect a 1-for-20 reverse split of our common stock (the "Reverse Split") and to reduce the number of authorized shares of our common stock to 20,000,000 from 150,000,000. Immediately following the effectiveness of the Reverse Split, there were approximately 2,869,739 shares of our common stock outstanding. Stockholders will receive a cash payment in lieu of any issuance of fractional shares. The number of shares of common stock issuable upon exercise or conversion of all outstanding options, warrants and convertible debt and the associated exercise or conversion prices will be adjusted accordingly for the Reverse Split.

At our annual meeting of stockholders held on May 22, 2014, our stockholders approved an amendment to our certificate of incorporation that would (1) effect a reverse split of our common stock at a ratio between 1:10 to 1:20 to be determined by the board of directors in its discretion and (2) if the reverse split is effected, decrease the number of shares of Common Stock that the Corporation is authorized to issue from 150,000,000 to the greater of (A) 20,000,000 and (B) the number of shares equal to three (3) times the sum of the number of all shares of our common stock outstanding and the number of shares of common stock issuable upon exercise or conversion of all outstanding options, warrants and convertible debt. Our stockholders further authorized the board of directors to determine the ratio at which the reverse split would be effected and the corresponding reduction in authorized shares of common stock by filing an appropriate amendment to our certificate of incorporation. Our board of directors authorized the ratio of the Reverse Split and corresponding reduction in authorized shares on June 6, 2014.

A copy of the amendment to our certificate of incorporation is attached as Exhibit 3.1 and is incorporated by reference herein.

ITEM 7.01 REGULATION FD DISCLOSURE

A copy of the press release issued by us on June 13, 2014 announcing the Reverse Split is furnished as Exhibit 99.1 and is incorporated by reference herein.

ITEM 8.01 OTHER ITEMS

On June 9, 2014 and June 10, 2014 presentations relating to our technology were made at the 2014 Annual Meeting of the Society of Nuclear Medicine. The presentations are attached as Exhibit 99.2 and 99.3 and are incorporated by reference herein.

ITEM 9.01 FINANCIAL STATEMENTS AND EXHIBITS

(d) Exhibits

Number	Title
3.1	Certificate of Amendment to the Second Amended and Restated Articles of Incorporation of Cellectar Biosciences, Inc.
99.1	Press Release dated June 13, 2014 entitled "Cellectar Biosciences Announces 1-for-20 Reverse Stock Split and Reduction in Authorized Shares of Common Stock"
99.2	Presentation entitled "A Phase 1 Study of 131I-CLR1404 in Patients with Relapsed or Refractory Advanced Solid Tumors; Dosimetry, Biodistribution, Pharmacokinetics and Safety"
99.3	Presentation entitled "Comparison of MRI and PET Tumor Volumes with 124I-CLR1404 PET/CT in Primary and Metastatic Brain Tumors"

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: June 13, 2014

CELLECTAR BIOSCIENCES, INC.

By: */s/ Chad J. Kolean*
Name: Chad J. Kolean
Title: Vice President and Chief Financial Officer

EXHIBIT INDEX

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CERTIFICATE OF AMENDMENT
TO
THE SECOND AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
CELLECTAR BIOSCIENCES, INC.

CELLECTAR BIOSCIENCES, INC. (the "Corporation"), a corporation organized and existing under of the General Corporation Law of the State of Delaware, does hereby certify:

FIRST: The name of the Corporation is Cellectar Biosciences, Inc.

SECOND: The Second Amended and Restated Certificate of Incorporation of the Corporation is hereby amended as follows.

1. By inserting the following paragraphs in Article FOURTH thereof immediately following the first paragraph of said Article FOURTH:

"Upon the effectiveness of the amendment to the Amended and Restated Certificate of Incorporation adding this paragraph thereto (the "Effective Time"), each share of Common Stock, par value $0.00001 per share issued and outstanding immediately prior to the Effective Time (the "Original Common Stock"), shall be reclassified into 1/20 of a share of Common Stock, such Common Stock to have the rights and powers set forth in the Certificate of Incorporation and under the General Corporation Law of the State of Delaware (the "Reclassification"). All shares of Common Stock issued to any holder of Original Common Stock as a result of the Reclassification shall be aggregated for the purpose of determining the number of shares of Common Stock to which such holder shall be entitled, and no fractional shares shall be issued in connection with the Reclassification.

Any stockholder who would otherwise be entitled to receive a fractional share of Common Stock as a result of the Reclassification shall receive in lieu thereof cash in an amount equal to such fraction multiplied by the fair market value of one share of Common Stock, based on the average of the high and low bid prices of the Common Stock as quoted on the Over-the-Counter Bulletin Board on the last trading day immediately preceding the Effective Time. No cash in lieu of any fractional share shall be paid to any stockholder until such stockholder shall have surrendered for transfer or otherwise accounted to the Corporation for the outstanding stock certificates entitling such stockholder to such cash.

At and after the Effective Time, outstanding certificates that prior thereto represented shares of Original Common Stock shall be deemed for all purposes to evidence ownership of and to represent that number of shares of Common Stock into which the shares previously represented by such certificates have been reclassified as herein provided (and the right to receive cash in lieu of any fraction of a share as provided herein). Until any such outstanding stock certificates have been surrendered for transfer or otherwise accounted for to the Corporation, the registered owner thereof on the books and records of the Corporation shall have and be entitled to exercise any voting and other rights with respect to, and receive any dividend and other distributions upon, the shares of Common Stock issued in respect of the Original Common Stock formerly evidenced by such certificates."; and

2. By amending and ratifying in its entirety the first paragraph of Article FOURTH as follows:

> "**Fourth.** The aggregate number of shares of stock that the Corporation shall have authority to issue is twenty million and seven thousand (20,007,000), of which twenty million (20,000,000) shares shall be designated "Common Stock" and seven thousand (7,000) shares shall be designated "Preferred Stock." Shares of Common Stock and Preferred Stock shall have a par value of $0.00001 per share."

THIRD: The foregoing amendment was duly adopted in accordance with the provisions of Section 242 of the General Corporation Law of the State of Delaware.

FOURTH: The foregoing amendment shall be effective at 5:00 pm eastern time on June 13, 2014.

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment to the Second Amended and Restated Certificate of Incorporation to be signed by Simon Pedder, its President and Chief Executive Officer, thereto duly authorized, this 10th day of June, 2014.

CELLECTAR BIOSCIENCES, INC.

By: */s/ Simon Pedder*
Simon Pedder
President and Chief Executive Officer

Cellectar Biosciences Announces 1-for-20 Reverse Stock Split and Reduction in Authorized Shares of Common Stock

MADISON, Wis., June 13, 2014, – Cellectar Biosciences, Inc. (OTCQX: CLRB), announced a 1-for-20 reverse stock split of its common stock, effective at the close of business today, as a first step in a planned listing of its common stock on the NASDAQ Capital Market.

Shares of Cellectar's common stock will trade on a post-split basis beginning on June 16, 2014. The Company's ticker symbol will remain unchanged, although a "D" will be placed on the ticker symbol, CLRB, for 20 business days to alert the public to the Reverse Split. The new CUSIP number for Cellectar's common stock post-reverse stock split will be 15117F 203.

At the effective time of the reverse stock split, every 20 shares of Cellectar's issued and outstanding common stock will automatically be combined into 1 issued and outstanding share of common stock without any change in the par value of the shares. This will reduce the number of outstanding common shares of Cellectar from approximately 57 million to approximately 2.8 million. In conjunction with the reverse stock split, Cellectar will decrease the number of its authorized shares of common stock from 150,000,000 to 20,000,000. Stockholders approved the reverse split and the reduction in authorized shares at the 2014 Cellectar Annual Meeting held on May 22, 2014. Additional information can be found in a Form 8-K to be filed with the Securities and Exchange Commission.

"We believe this reverse split will make an investment in Cellectar both viable and more appealing to a broader institutional investment community," commented Dr. Simon Pedder, president and chief executive officer of Cellectar. "Coupled with a successful capital raise, the next prerequisite, and planned NASDAQ listing, we should be able to meaningfully increase stockholder value as we execute our clinical programs and advance our pipeline of promising cancer-targeting imaging and therapeutic technology."

Proportionate voting rights and other rights of common stockholders will not be affected by the reverse stock split, other than as a result of the cashing out of fractional shares. Stockholders who would otherwise hold a fractional share of common stock will receive a cash payment in lieu of a fractional share. Please direct any questions you might have regarding payments for fractional shares to your broker or our transfer agent, American Stock Transfer & Trust Company, by calling (718) 921-8317.

About Cellectar Biosciences, Inc.

Cellectar Biosciences is developing agents to detect, treat and monitor a broad spectrum of cancers. Using a novel phospholipid ether analog (PLE) platform technology as a targeted delivery and retention vehicle, Cellectar's compounds are designed to be selectively taken up and retained in cancer cells including cancer stem cells. With the ability to attach both imaging and therapeutic agents to its proprietary delivery platform, Cellectar has developed a portfolio of product candidates engineered to leverage the unique characteristics of cancer cells to "find, treat and follow" malignancies in a highly selective way. I-124-CLR1404 is a small-molecule, broad-spectrum, cancer-targeted PET imaging agent currently being evaluated in a Phase II glioblastoma imaging trial. Additionally, multiple investigator-sponsored Phase I/II clinical trials are ongoing across 11 solid tumor indications. I-131-CLR1404 is a small-molecule, broad-spectrum, cancer-targeted molecular radiotherapeutic that delivers cytotoxic radiation directly and selectively to cancer cells including cancer stem cells. A Phase Ib dose-escalation trial of I-131-CLR1404 in patients with advanced solid tumors was completed in the first quarter of 2014 and results presented at the American Society of Clinical Oncology (ASCO) 2014 Annual Meeting. CLR1502 is a preclinical, cancer-targeted, non-radioactive optical imaging agent for intraoperative tumor margin illumination and non-invasive tumor imaging. For additional information please visit www.cellectar.com

INVESTOR CONTACT

Kate McNeil, Vice President of IR, PR & Corporate Communications
Cellectar Biosciences, Inc.
Phone: (347) 204-4226
Email: kmcneil@cellectar.com

This news release contains forward-looking statements. You can identify these statements by our use of words such as "may," "expect," "believe," "anticipate," "intend," "could," "estimate," "continue," "plans," or their negatives or cognates. These statements are only estimates and predictions and are subject to known and unknown risks and uncertainties that may cause actual future experience and results to differ materially from the statements made. These statements are based on our current beliefs and expectations as to such future outcomes. Drug discovery and development involve a high degree of risk. Factors that might cause such a material difference include, among others, uncertainties related to the ability to raise additional capital, uncertainties related to the ability to attract and retain partners for our technologies, the identification of lead compounds, the successful preclinical development thereof, the completion of clinical trials, the FDA review process and other government regulation, our pharmaceutical collaborators' ability to successfully develop and commercialize drug candidates, competition from other pharmaceutical companies, product pricing and third-party reimbursement. A complete description of risks and uncertainties related to our business is contained in our periodic reports filed with the Securities and Exchange Commission including our Form 10-K for the year ended December 31, 2013. These forward-looking statements are made only as of the date hereof, and we disclaim any obligation to update any such forward-looking statements.

A Phase 1 Study of 131I-CLR1404 in Patients with Relapsed or Refractory Advanced Solid Tumors: Dosimetry, Biodistribution, Pharmacokinetics, and Safety

Joseph J Grudzinski[1,2], Benjamin Titz[1,2], Kevin Kozak[1], William Clarke[1], Ernest Allen[1], LisaAnn Trembath[1], Michael Stabin[4], John Marshall[5], Steve Y. Cho[6], Terence Z. Wong[7], Joanne Mortimer[8], Jamey P Weichert[1,3]

[1]Cellectar Biosciences, Inc. [2]Department of Medical Physics, University of Wisconsin SMPH [3]Department of Radiology, University of Wisconsin [4]Vanderbilt University [5]Georgetown University [6]Johns Hopkins Hospital [7]Duke University Medical Center [8]City of Hope

ABSTRACT

^{131}I-CLR1404 is a small molecule that combines a tumor-targeting moiety with a therapeutic radioisotope. **The primary aim of this study was to determine the administered radioactivity expected to deliver 40 cGy of dose to the marrow. The secondary aims of the study were to determine the pharmacokinetic (PK) and safety profiles of 131I-CLR1404.** **Methods:** Eight subjects with refractory or relapsed advanced solid tumors were treated with a single injection of 370 MBq of ^{131}I-CLR1404. Whole body planar nuclear medicine scans were performed at 15-35 minutes, 4-6, 18-24, 48, 72, 144 hours, and 14 days post injection. Optional single photon emission computed tomography imaging was performed on two patients 6 days post injection. Clinical laboratory parameters were evaluated in blood and urine. Plasma PK was evaluated on ^{127}I-CLR1404 mass measurements. To evaluate the renal clearance of ^{131}I-CLR1404, urine was collected for 14 days post injection. Absorbed dose estimates for target organs were determined using the RADAR method with the OLINDA/EXM software. **Results:** Single administrations of 370 MBq of ^{131}I-CLR1404 were well tolerated by all subjects. No severe adverse events were reported and no adverse event was dose-limiting. Plasma CLR1404 concentrations declined in a bi-exponential manner with a mean t½ value of 822 hours. Mean Cmax and AUC(0-t) values were 72.2 ng/mL and 15753 ng·hr/mL, respectively. An administered activity of approximately 740 MBq is predicted to deliver 40 cGy to marrow. **Conclusions:** Preliminary data suggest that ^{131}I-CLR1404 is well tolerated and may have unique potential as an anti-cancer therapeutic agent.

MATERIALS & METHODS

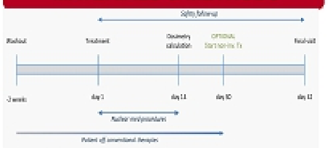


Figure 1: Flowchart describing the clinical study

Dosimetry and Radiologic Biodistribution Analysis: Total urine was collected for radiologic biodistribution analysis for the first 14 days of the study. Whole body planar imaging was performed at the following time points for assessment of total body and organ radiation dosimetry: 15 – 35 minutes, 4-6 hours, 18-24 hours, 48 ± 6 hours, 72 ± 6 hours, 144 ± 6 hours, and Day 14 ± 1 post infusion.

Biodistribution data were analyzed using the Organ Level INternal Dose Assessment (OLINDA) methodology to produce time/activity curves and generate organ specific radiation absorbed doses from a 10 mCi injection of ^{131}I-CLR1404. These data, along with total urine collection for up to 14 days, were used to extrapolate and predict organ specific and total body radiation absorbed doses from therapeutic injections of ^{131}I-CLR1404.

Pharmacokinetics: A pharmacokinetic assessment of the plasma concentration of the parent compound (^{127}I-CLR1404) was performed using a validated HPLC method with MS/MS detection (LLOQ 2.00 ng/mL).

Analyses of plasma ^{127}I-CLR1404 CLR1404 concentration-time data were conducted using non-compartmental methods and the pharmacokinetics of CLR1404 were assessed by determining maximum plasma concentration (Cmax), time to Cmax (Tmax), area under the concentration curve from 0 to 144 hours [AUC(0-144hr)], area under the concentration curve from time 0 to time t (t is the time of last quantifiable concentration; t = 1008 hr) [AUC(0-t)], plasma half-life ($t_{½}$), effective plasma half-life ( ) and apparent terminal phase rate constant (λz), clearance (CL), volume of distribution (Vd), and volume of distribution at steady-state (Vss).

Safety: Safety was assessed by adverse event (AE) monitoring, clinical laboratory tests (hematology, chemistry, lipids, and urinalysis), electrocardiogram (ECGs), vital signs (including temperature and SaO2), physical exams, determination of ECOG performance status, serum pregnancy test for females of child-bearing potential, medical history and medication review.

Table 1: *Patient Information. Details about the patients enrolled in the study.*

Patient	Center	Age	Gender	Race or Ethnicity	Primary Solid tumor	Metastatic sites	Prior chemotherapy	Prior hormonal, immunological, biological and other therapy
[illegible]	Georgetown	[illegible]	Female	White	Colon	[illegible]	FOLFOX [illegible]	[illegible]
[illegible]	Georgetown	[illegible]	Male	Black	Colon	Lymph node, Kidney, Liver, Lung	[illegible]	
[illegible]	Georgetown	[illegible]	Male	White	Colon	Lymph node	[illegible]	
[illegible]	Johns Hopkins	[illegible]	Male	White	Esophageal	Lymph node, Liver, Lung	[illegible]	
[illegible]	Duke	[illegible]	Male	White	Colon	Lung	[illegible]	[illegible]
[illegible]	Duke	[illegible]	Male	White	Prostate	Bone	[illegible]	[illegible]
[illegible]	City of Hope	[illegible]	Female	[illegible]	[illegible]	[illegible]		[illegible]
[illegible]	City of Hope	[illegible]	Male	White	Prostate	Lung, Bone		[illegible]

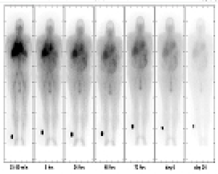


Figure 2: Whole body conjugate-view planar images for patient 301. Images are shown for 15-30 minutes, 4, 24, 48, 72 hours, 6 and 14 days post injection, respectively. Because the agent is metabolized in the hepatobiliary system, there is evidence of ^{131}I-CLR1404 within the liver and intestines at relatively late time points.

RESULTS

Table 2: Summary of the Dosimetry results. Statistical summary of the eight patients' dosimetry calculations.

	Average		±SD		CV%
	mGy/MBq	rem/mCi	mGy/MBq	rem/mCi	
Adrenals	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Brain	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Breasts	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Gallbladder Wall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
LLI Wall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Small Intestine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Stomach Wall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ULI Wall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Heart Wall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Kidneys (all subjects)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Kidneys (excluding [illegible])	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Liver	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Lungs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Muscle	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Ovaries	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Pancreas	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Red Marrow	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Osteogenic Cells	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Skin	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Spleen	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Testes	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Thymus	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Thyroid	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Urinary Bladder Wall	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Uterus	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total Body	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Effective Dose	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

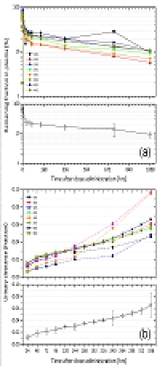


Figure 3: Plasma PK (a) and fraction of urinary clearance (b). The top and bottom panels represent the individual and mean (±SD) data, respectively.

Table 3: Summary of results from the pharmacokinetic analysis

Subject Number	C_{max} (ng/mL)	T_{max} (hr)	AUC_{0-144} (ng·hr/mL)	AUC_{0-t} (ng·hr/mL)	$AUC_{0-\infty}$ (ng·hr/mL)	λz (1/hr)	$t_{1/2}$ (hr)	$t_{1/2,eff}$ (hr)	CL (L/hr)	Vd (L)	Vss (L)
N	8	8	8	8	8	8	8	8	8	8	8
Mean	72.2	0.302	3430	15758	16703	0.000835	822	355	0.0118	13.6	13.6
SD	11.5	0.07	574	3566	3614	0.000132	101	5.8	0.0035	2.9	2.7
Min	54.6	0.25	2536	11260	10683	0.000712	685	349	0.00804	10.5	10.8
Median	71.6	0.258	3501	15433	17374	0.000825	841	356	0.0106	13.2	12.9
Max	90.5	0.417	4010	22206	21983	0.00104	974	361	0.0165	17.9	17.5
CV%	16	23	17	23	21	13	12	1.5	27	21	20

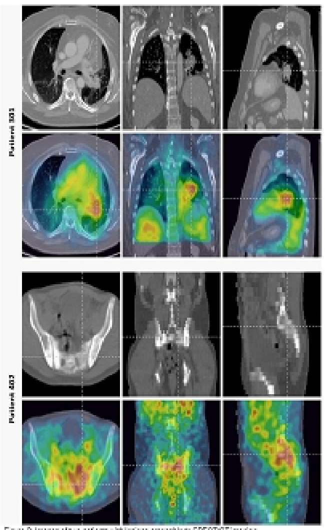


Figure 2: Images of two patients with lesions amenable to SPECT/CT imaging

SUMMARY

- An administered activity of approximately 740 MBq (20 mCi) is predicted to deliver 40 cGy to marrow.
- Single doses of 10 mCi of ^{131}I-CLR1404 were well tolerated when administered to subjects with advanced cancers. There were no SAEs reported and all AEs were considered minimal, manageable and not dose limiting.
- After an intravenous administration of 10 mCi of ^{131}I-CLR1404 (0.3 mg total mass dose), CLR1404 declined in a bi-exponential manner with a mean t½ value of 822 hours.
- Mean C_{max} and $AUC_{(0-t)}$ values were 72.2 ng/mL and 15753 ng·hr/mL, respectively.

Study funded by Cellectar Biosciences, Inc.

Comparison of MRI and PET Tumor Volumes with ^{124}I-CLR1404 PET/CT in Primary and Metastatic Brain Tumors

Lance T. Hall, MD
University of Wisconsin

Benjamin Titz, Joseph Grudzinski, Emmaline Stilp, Christine Jaskowiak, Stephanie Rice, Jamey Weichert, John Kuo

DEPARTMENT OF
RADIOLOGY
University of Wisconsin
School of Medicine and Public Health

Disclosures

- **NIH/NCI: 1 R01 CA158800** (PI: Hall/Weichert)
- UW ICTR from **NIH/NCATS: UL1TR000427** (PI: Hall)
- UW Carbone Cancer Center from **NIH/NCI: P30CA014520** (PI: Hall)

- Lance Hall -- No financial COI
  - Physician sponsor of IND for ^{124}I-CLR1404
- Jamey Weichert – inventor of CLR1404 and founding member of Cellectar Biosciences, Inc
- Benjamin Titz & Joseph Grudzinski – employees of Cellectar Biosciences, Inc

Brain Tumor Imaging - Limitations

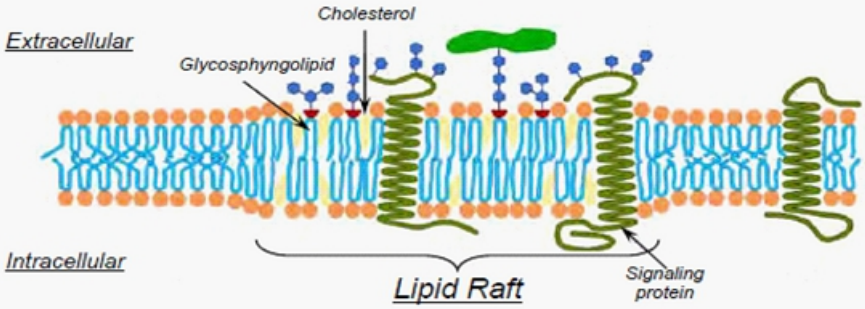
- Incomplete delineation of tumor infiltration
  - Affects surgical resection & XRT planning & survival
- Non-specificity for tumor vs necrosis or edema
  - Biopsy site planning & resection of eloquent brain
- Differentiating tumor recurrence from pseudoprogression (PP)
  - Huge problem w/ Temozolomide & newer agents
- Predict tumor response to Tx
  - Prospective response & individual tumor dosimetry

CLR1404 (aka "NM404") Background

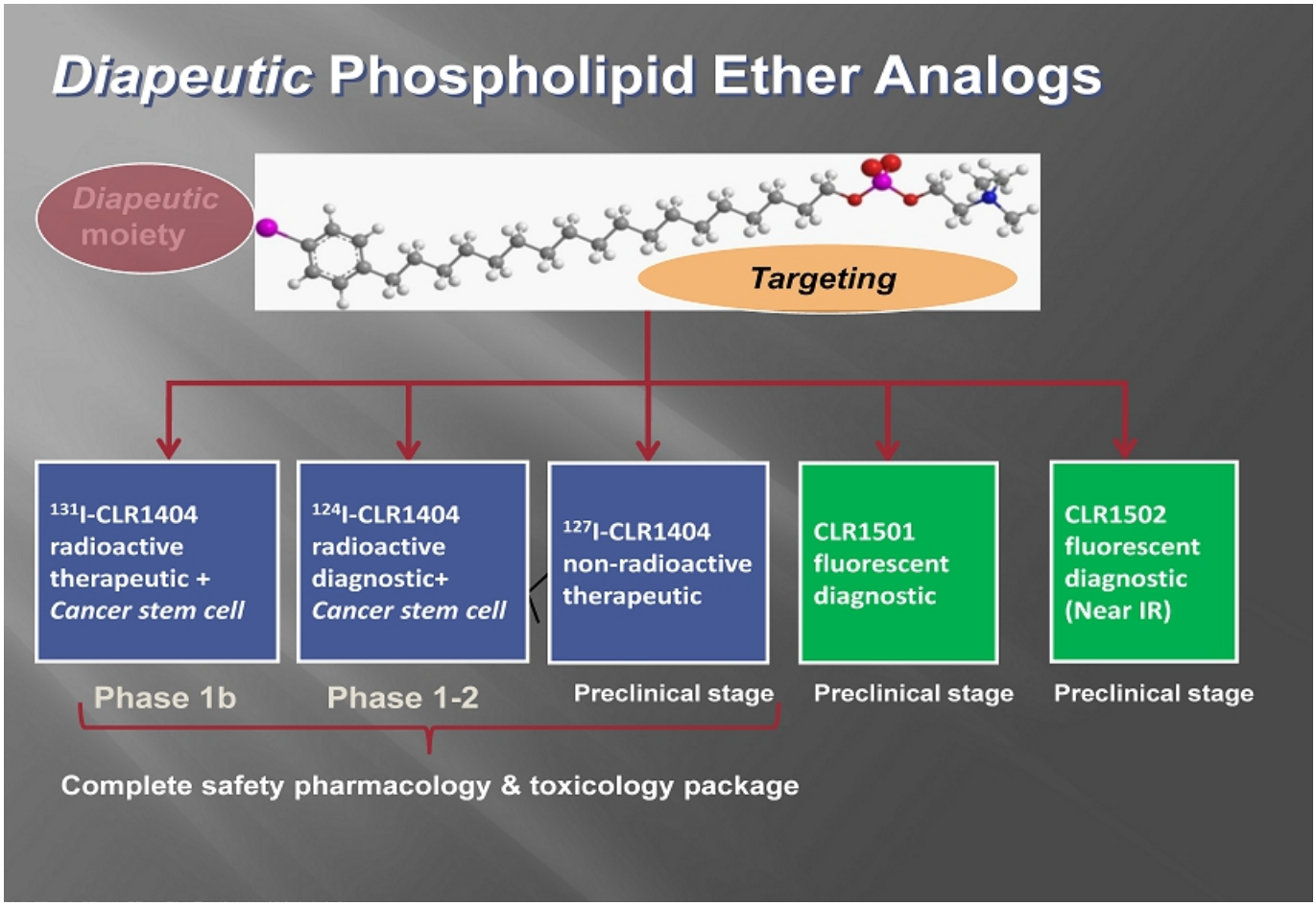
- Phospholipid ether (PLE) analog
- Enters malignant cells via membrane lipid rafts
  - Over expressed in malignant cells (6 – 10x)
- Tumor specific uptake & prolonged retention in >50 preclinical models
  - Including gliomas
- Isoteric iodine substitution
  - ^{124}I- for molecular/PET imaging
  - ^{131}I- for therapy
  - Optical imaging agents also being developed

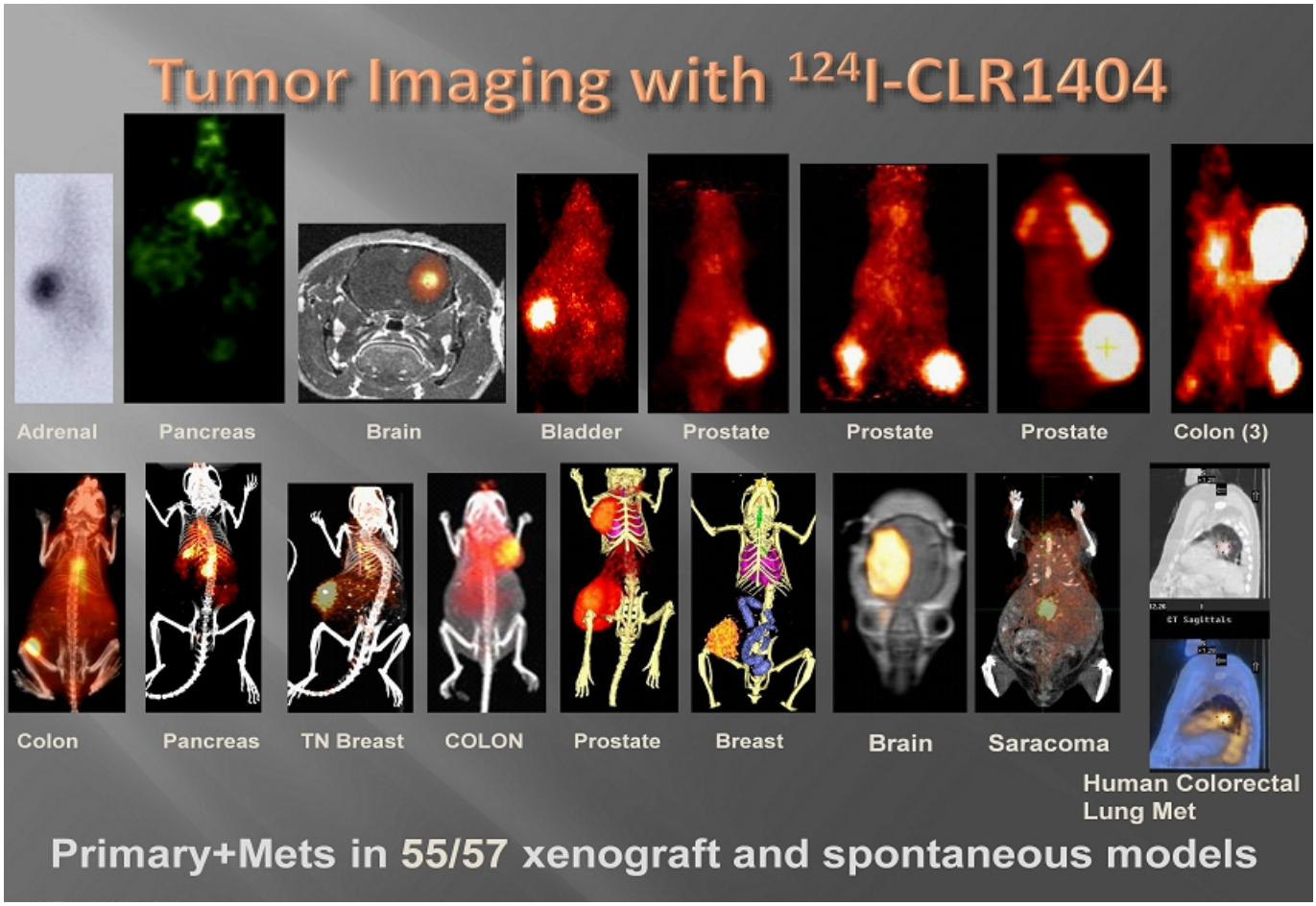
"Diapeutic"

Lipid Rafts



- Lipid rafts are specialized microdomains of plasma membrane that are enriched in cholesterol and glycosphingolipids
- Lipid rafts serve as molecular platforms that spatially organize molecules for specific signaling pathways including those involved in regulation of apoptosis and cell proliferation (e.g. growth factor receptors, Akt, TNF receptors)


Diapeutic Phospholipid Ether Analogs
Diapeutic moiety
Targeting
131I-CLR1404 radioactive therapeutic + Cancer stem cell
124I-CLR1404 radioactive diagnostic+ Cancer stem cell
127I-CLR1404 non-radioactive therapeutic
CLR1501 fluorescent diagnostic
CLR1502 fluorescent diagnostic (Near IR)
Phase 1b
Phase 1-2
Preclinical stage
Preclinical stage
Preclinical stage
Complete safety pharmacology & toxicology package


Tumor Imaging with 124I-CLR1404
Adrenal
Pancreas
Brain
Bladder
Prostate
Prostate
Prostate
Colon (3)
Colon
Pancreas
TN Breast
COLON
Prostate
Breast
Brain
Saracoma
Human Colorectal
Lung Met
Primary+Mets in 55/57 xenograft and spontaneous models

Objectives

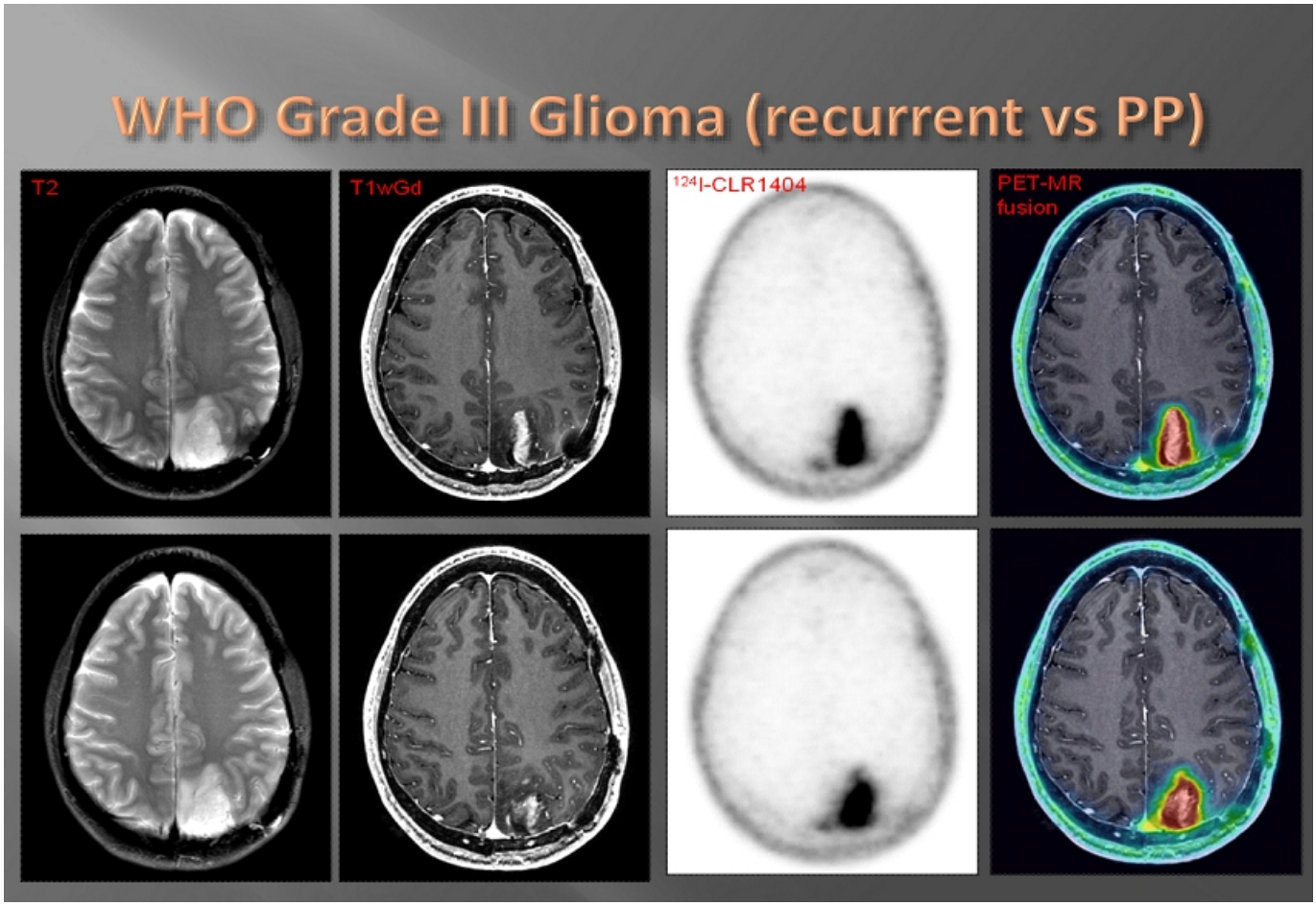
- Describe first successful use of ^{124}I-CLR1404 in humans with brain tumors
  - Avidity in brain tumors
  - SUV and Tumor to Background Ratios
  - Compare PET and MRI
    - Tumor volumes
    - Concordant and discordant tumor regions

Methods

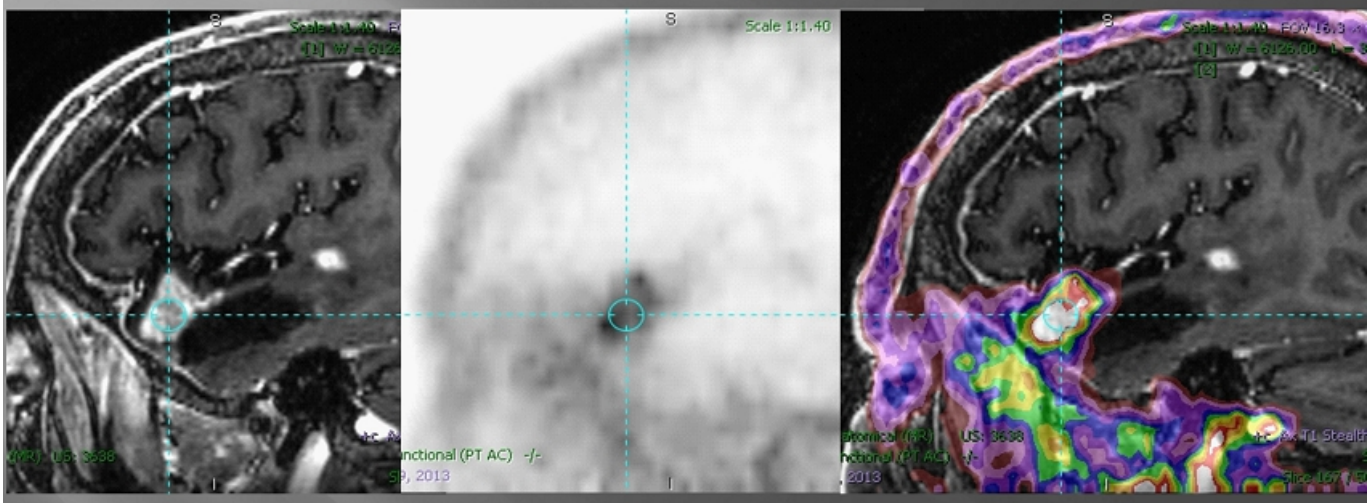
- 16 pts with brain tumors
  - 1 new dx (WHO Gr IV)
  - 11 previously tx'd gliomas (WHO Gr II – IV)
  - 3 previously tx'd metastases
  - 1 previously tx'd medulloblastoma
- 2 or 5 mCi (74 or 185 MBq) ^{124}I-CLR1404 iv
- PET/CT at 6-, 24-, and 48-hours after injection
  - 2D, list-mode, 90 minutes per scan
- Qualitative review of PET tumor uptake & MRI signal
- PET & MRI tumor volumes and SUVs and tumor-background ratios (T:B)
  - Amira segmentation to define tumor volumes
  - "mirror-image" tumor ROI placed in contralateral normal hemisphere
- 14 pts followed to surgery or w/ serial MRI ≥ 6 months

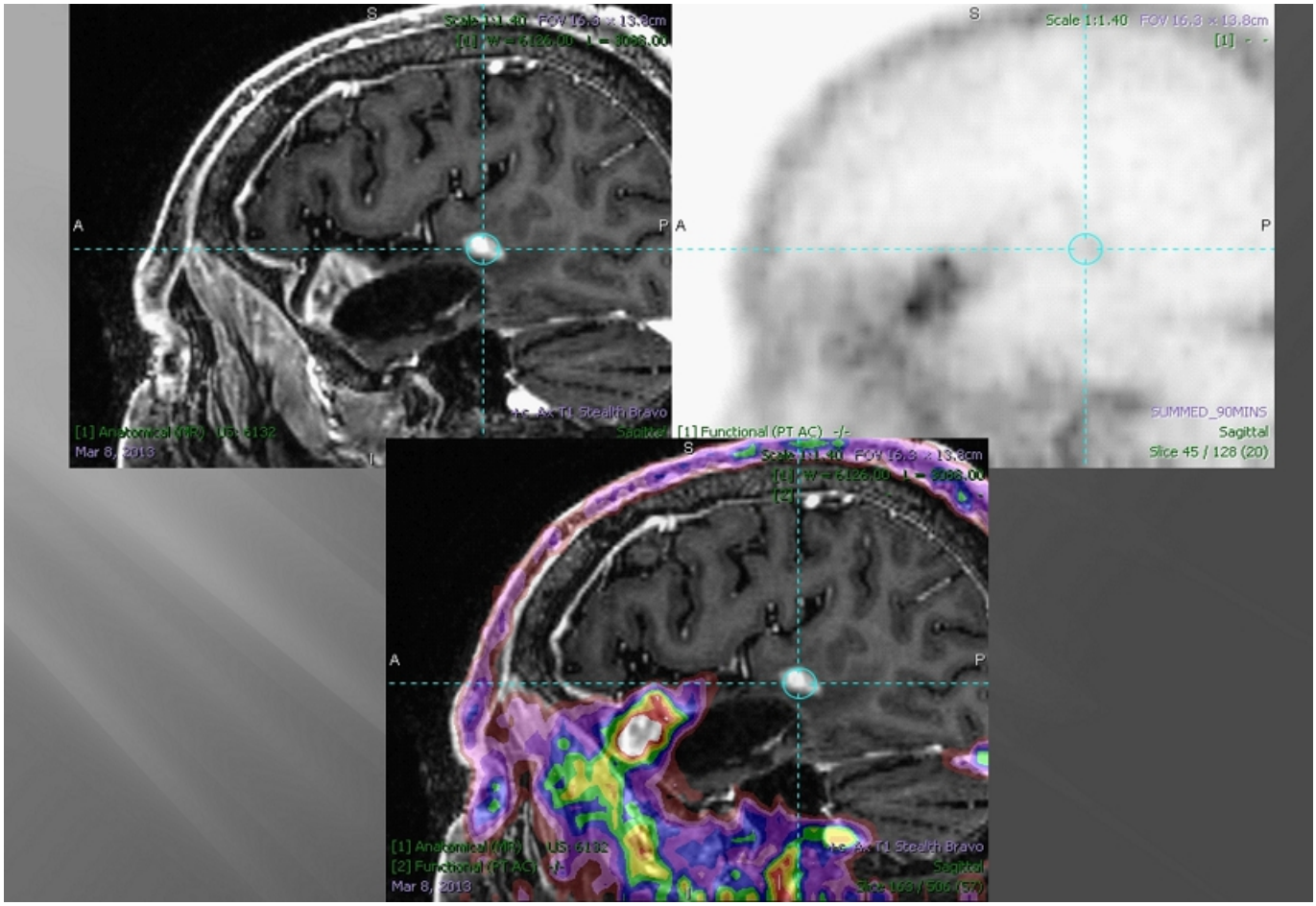
Results

- No uptake in normal brain
- Uptake in major vascular structures
  - Not in all areas of breakdown of BBB
- 12/16 pts had avid tumor uptake
  - 4 pts w/ recurrence vs PP had no uptake
  - Tumor uptake typically increases over time
- Both areas of concordant & discordant PET uptake and MRI enhancement

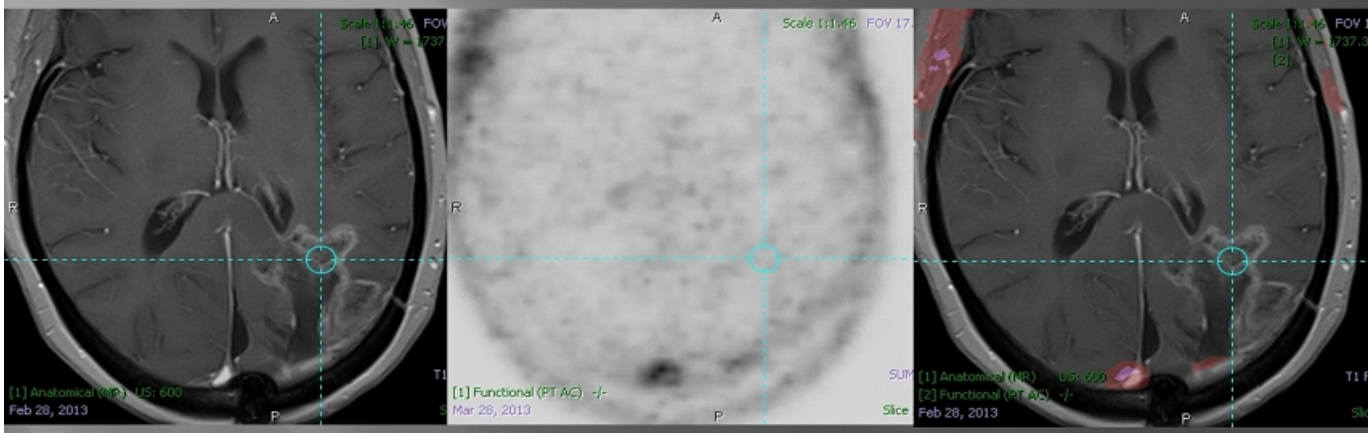

WHO Grade III Glioma (recurrent vs PP)
T2
T1wGd
124I-CLR1404
PET-MR fusion

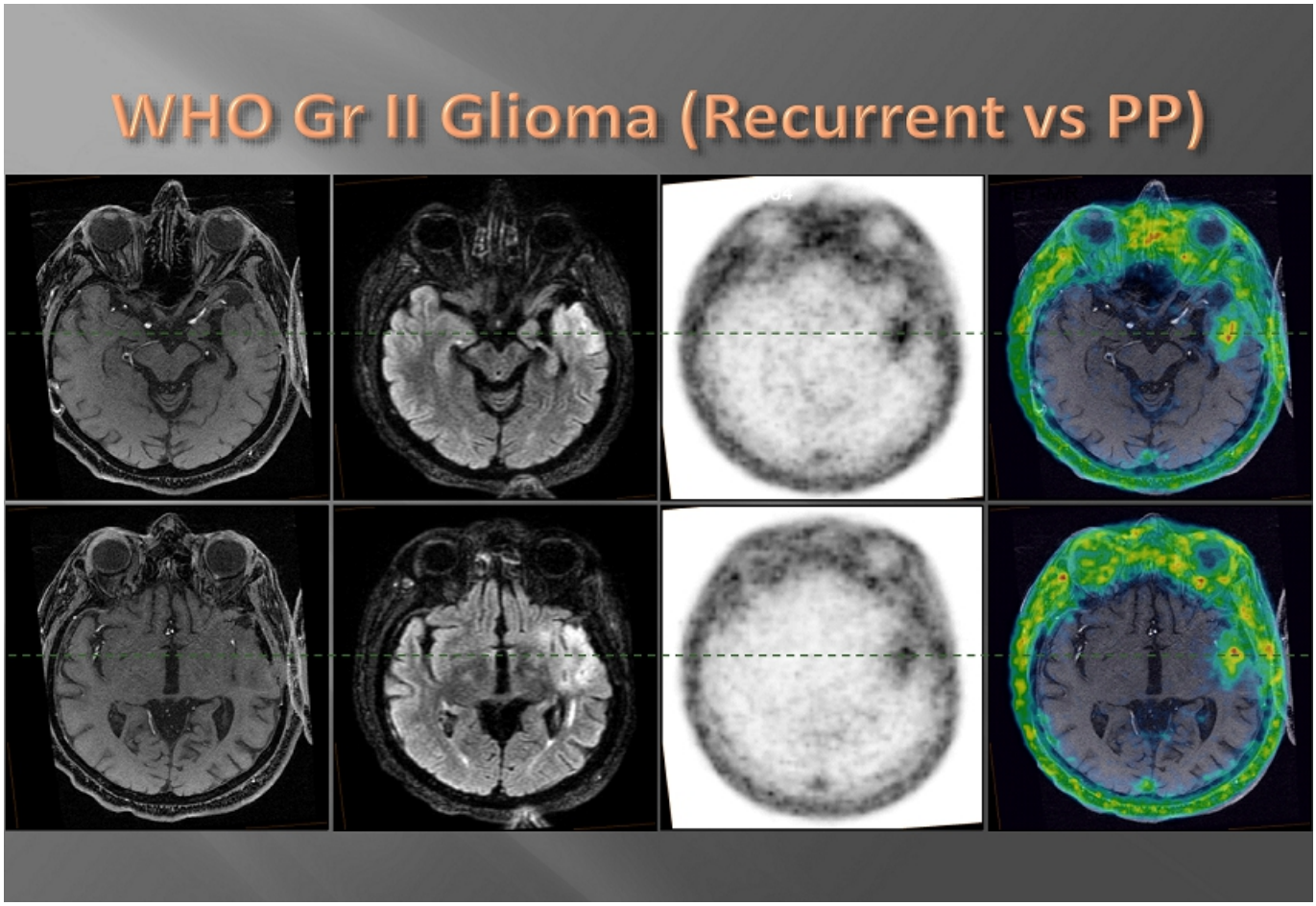
WHO Gr IV Glioma (recurrent vs PP)

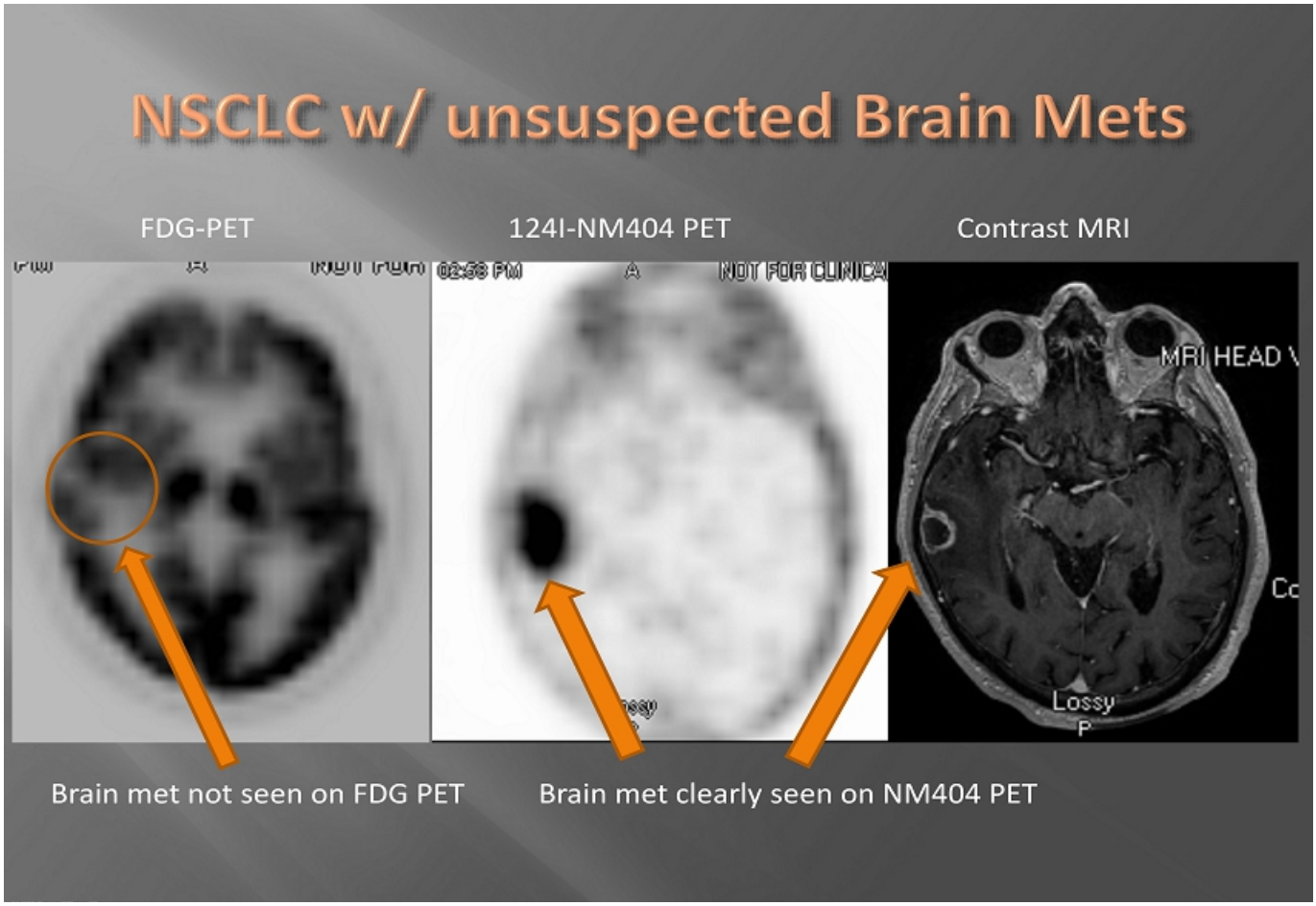


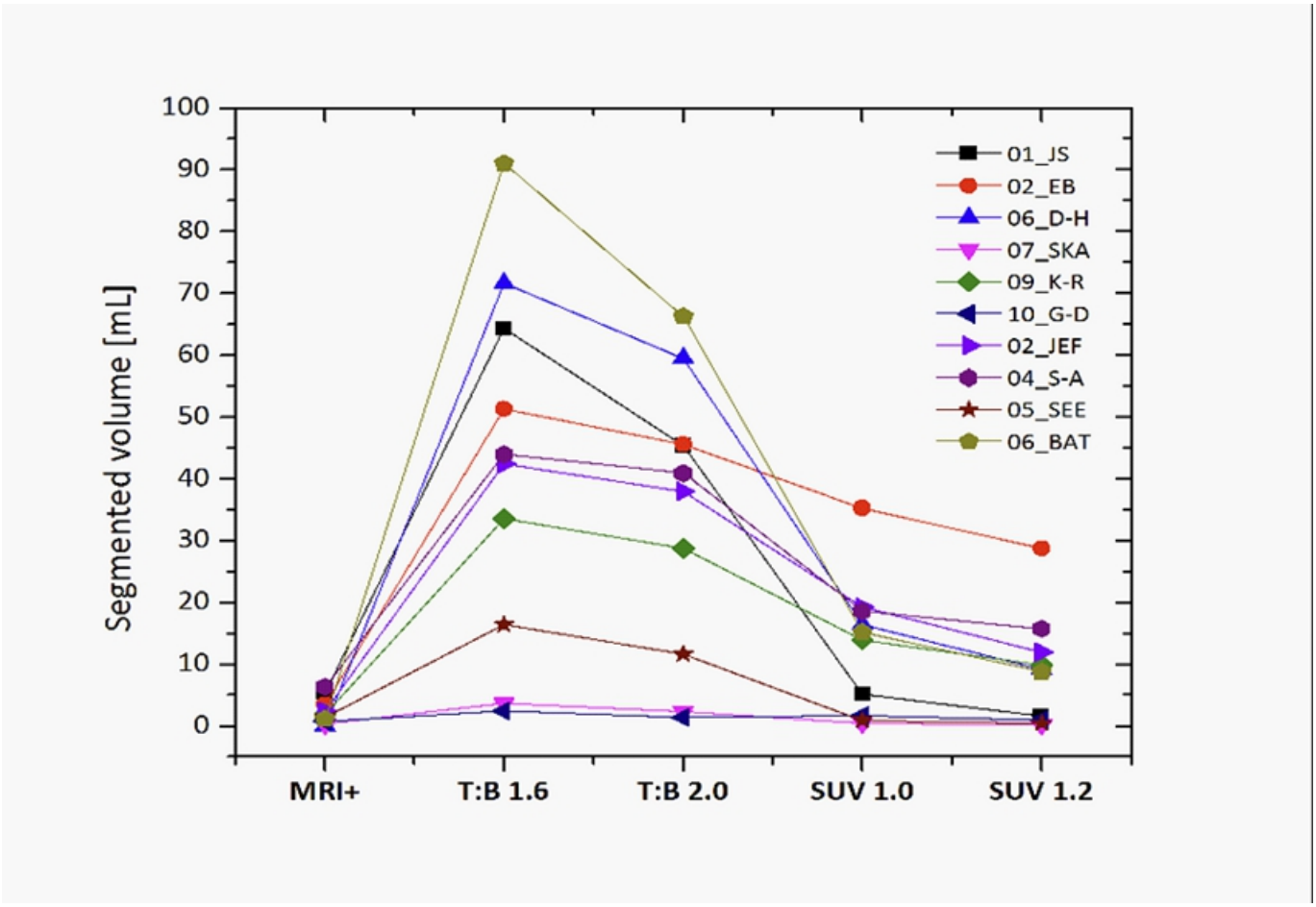

S
A
P
SUMMED_90MINS
Sagittal
Slice 45 / 128 (20)
[1] Functional (PT AC) -/-
[1] Anatomical (MR) US: 6132
[2] Functional (PT AC) -/-
Mar 8, 2013
Sagittal

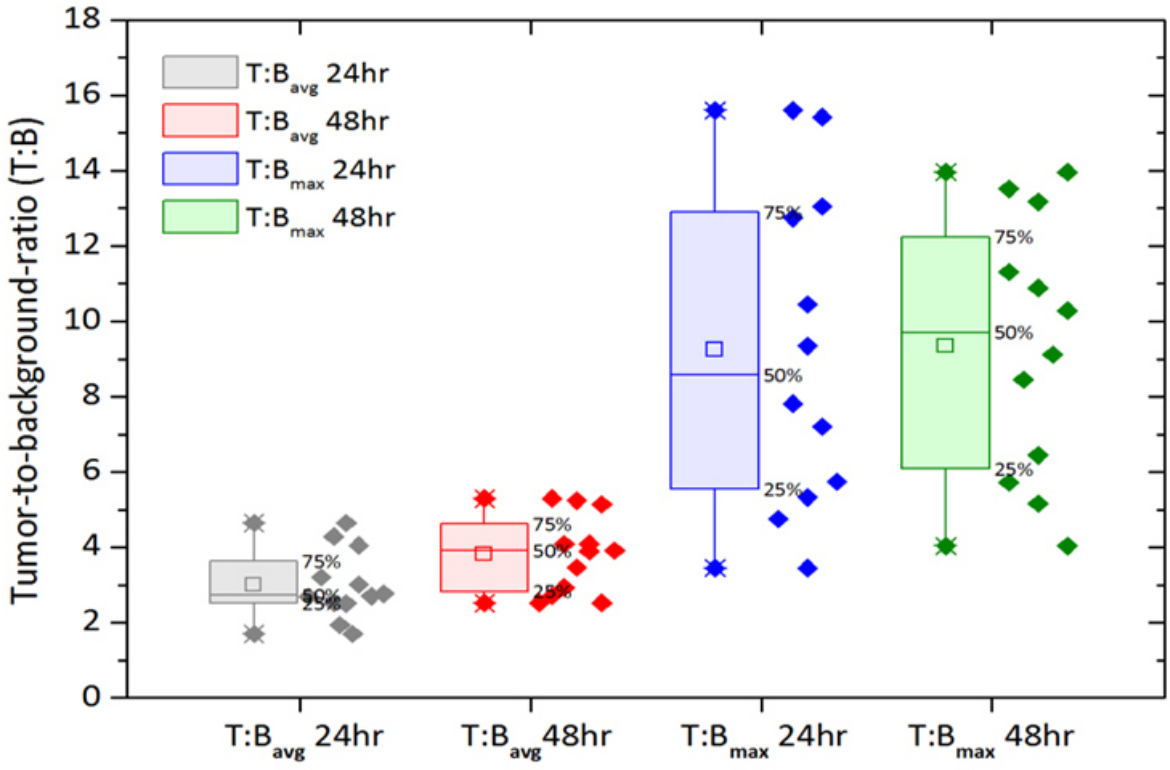
WHO Gr IV Glioma (Recurrent vs PP)




WHO Gr II Glioma (Recurrent vs PP)


NSCLC w/ unsuspected Brain Mets
FDG-PET
124I-NM404 PET
Contrast MRI
NOT FOR CLINICA
MRI HEAD
Lossy
Brain met not seen on FDG PET
Brain met clearly seen on NM404 PET


Segmented volume [mL]
100
90
80
70
60
50
40
30
20
10
0
MRI+
T:B 1.6
T:B 2.0
SUV 1.0
SUV 1.2
01_JS
02_EB
06_D-H
07_SKA
09_K-R
10_G-D
02_JEF
04_S-A
05_SEE
06_BAT


Tumor-to-background-ratio (T:B)
T:B$_{avg}$ 24hr
T:B$_{avg}$ 48hr
T:B$_{max}$ 24hr
T:B$_{max}$ 48hr
75%
50%
25%
0
2
4
6
8
10
12
14
16
18
T:B$_{avg}$ 24hr
T:B$_{avg}$ 48hr
T:B$_{max}$ 24hr
T:B$_{max}$ 48hr

Conclusion

- ^{124}I-CLR1404 successfully images primary and metastatic brain tumors in humans
- PET tumor volumes larger than MRI + Gad
- There is significant tumor to background uptake and prolonged retention
- Additional functional tumor info provided
- Potential for use as its own biomarker for targeted molecular radiotherapy


THANK YOU!
DEPARTMENT OF
RADIOLOGY
University of Wisconsin
School of Medicine and Public Health