



german
science day

02. Februar 2012
Berlin

Fight Cancer! Eine Initiative der Deutschen Biotechnologie

Diagnostik & Personalisierte Medizin:

“Guiding targeted therapies through diagnostics”

Professor Olaf G Wilhelm, MD, PhD CEO and co-founder of WILEX

WILEX
Focused Cancer Therapies

- **Oncology-focused biopharmaceutical company**
- **Product candidates with strong competitive profiles**
- **Important clinical and commercial milestones in the next months**
- **Integrative approach through combination of therapeutics and diagnostics**

Development success

Phase I II III

REDECTANE®

RENCAREX®

MESUPRON®

WX-554

Significant sales potential

- REDECTANE® ~ \$100m
- RENCAREX® ~ \$500m
- MESUPRON® ~ \$1bn

Deals & Alliances










Products & Technologies

OncogeneScience



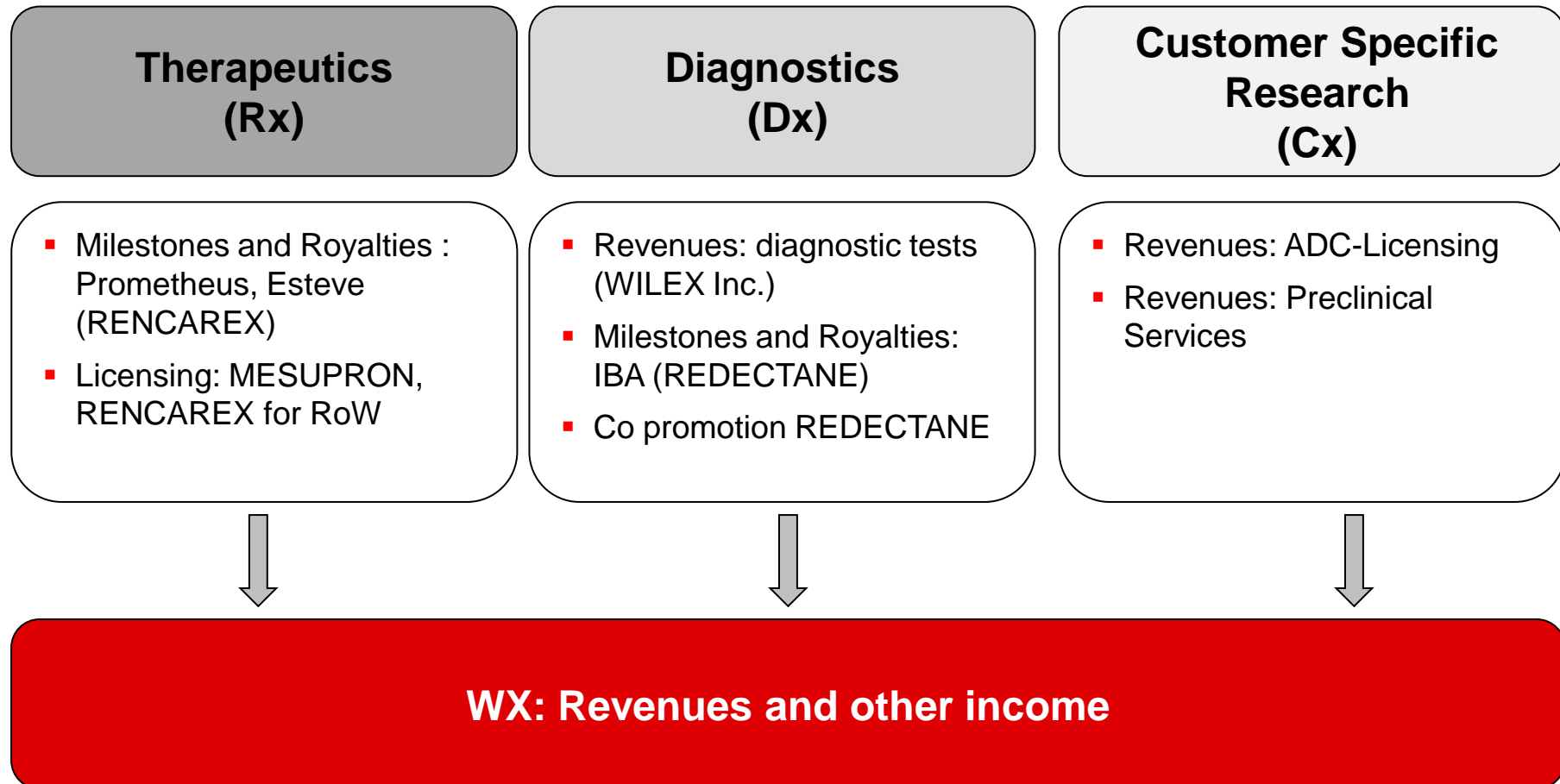
Therapeutics (Rx) + Diagnostics (Dx) + Customer Specific Research (Cx)

Broad portfolio and strong partners

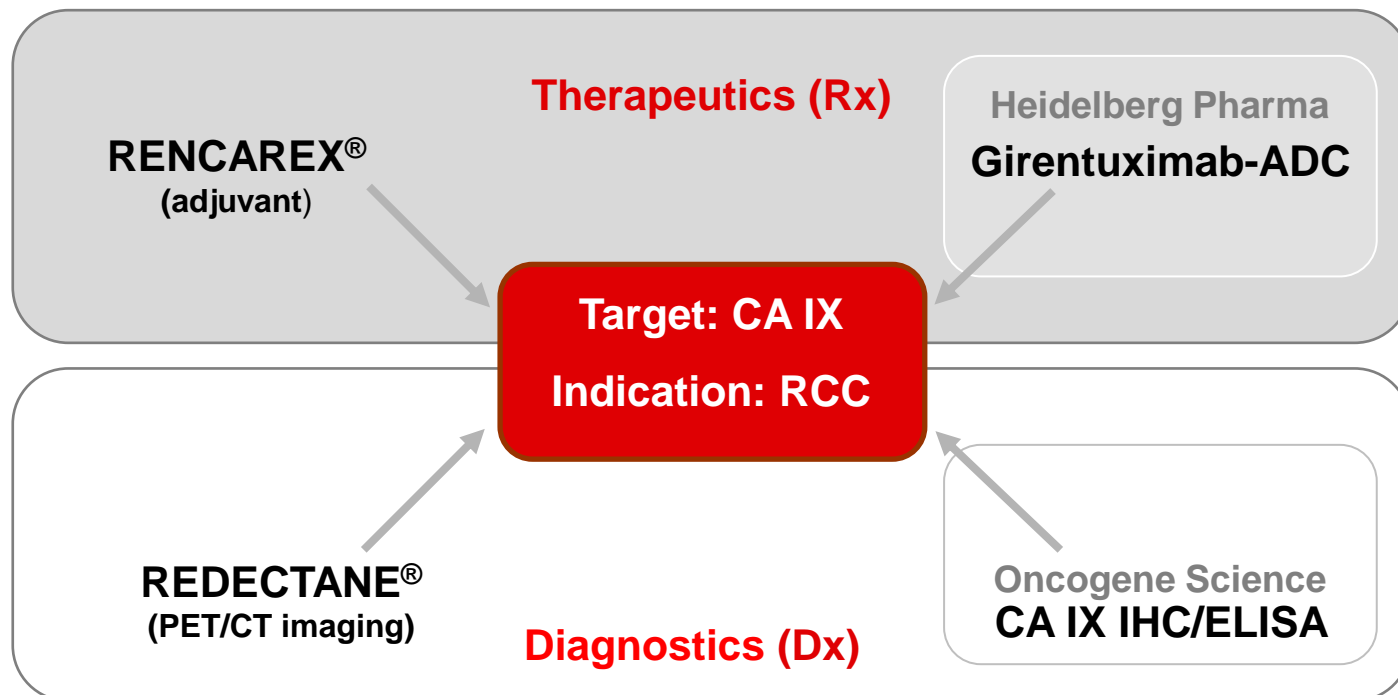
Product	Technology	Indication	Research	Pre-clinical	Clinical development			Market	Partner
					Phase I	Phase II	Phase III		
REDECTANE®	Antibody (diagnostic)	Renal mass	→					 (ww**)	
RENCAREX®	Antibody (therapeutic)	non-metast. ccRCC*	→					 (Southern Europe)  PROMETHEUS* (USA)	
MESUPRON®	uPA inhibitor	Pancreatic cancer	→						
		Breast cancer	→						
WX-554	MEK inhibitor	Cancer	→					 (ww)	
WX-037	PI3K inhibitor	Cancer	→					 (ww)	
2 Antibodies		Cancer	→					 (ww)	
ADC Platform	Antibody drug conjugates	Cancer	→					WILEX Group	
Diagnostic tests	ELISA/IHC	HER-2, CAIX, uPA, PAI-1, EGFr; VEGF etc.	→					 WILEX Group	

*clear cell Renal Cell Carcinoma, non-metastatic, ** worldwide

→ Realisation of the commercialisation strategy



- Focussed on target and indication with various mode of actions for personalised cancer treatment
- CA IX as an example for an integrative approach through combination of therapeutics and diagnostics



What is Carbonic Anhydrase IX (CAIX) and what does it do?

- CAIX is a cell surface protein involved in regulation of extracellular and intracellular pH
- Creates a microenvironment conducive for tumor growth and metastatic spread
- CAIX expression is strongly regulated by the transcription factor, hypoxia inducible factor (HIF-1)
- CAIX is a biomarker for hypoxia



Diagnostic imaging

REDECTANE®: Diagnosis of clear cell renal cell cancer (ccRCC)

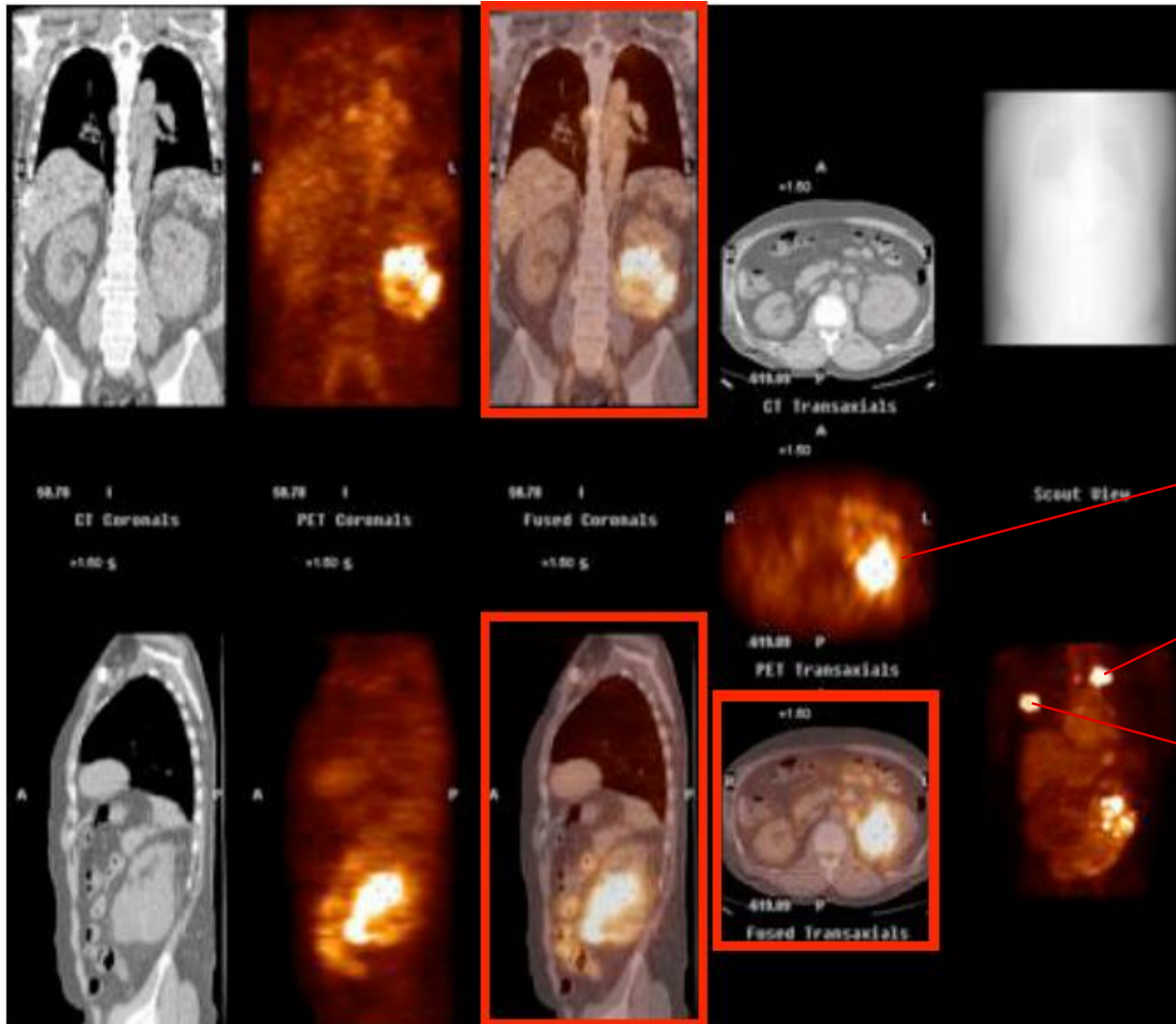
- Approx. 273,500 new cases of kidney cancer each year worldwide
- Clear cell renal cell cancer (ccRCC) is the most prevalent form of kidney cancer
- Current ccRCC patient management for a surgery decision is typically based on:
 - lesion size and
 - presumption of malignancy (ascertained by anatomical imaging)*
- Current standard of contrast-enhanced CT provides poor specificity
- Urologists utilise all available clinical information as part of patient management

*AUA guideline

- **Girentuximab (cG250) specifically and selectively binds to CAIX***
 - CAIX is constitutively upregulated in >95% of ccRCC
 - Not expressed by benign tumours such as oncocytoma and angiomyolipoma
- **Early studies in Nijmegen with ¹³¹I-cG250 show excellent specific tumour targeting**
 - Primary renal tumour and metastases visualised with radioscintigraphy
- **Concept of using ¹²⁴I-labelled girentuximab (REDECTANE®) developed by MSKCC/LICR**
- **Positive proof-of-concept study**
 - Ability to detect ccRCC malignancies pre-operatively confirmed
- **Pivotal study protocol (REDECT) developed with FDA input**
 - SPA approved by FDA

* CAIX=Carbonic Anhydrase 9

REDECTANE[®] detects primary tumour and distant metastases



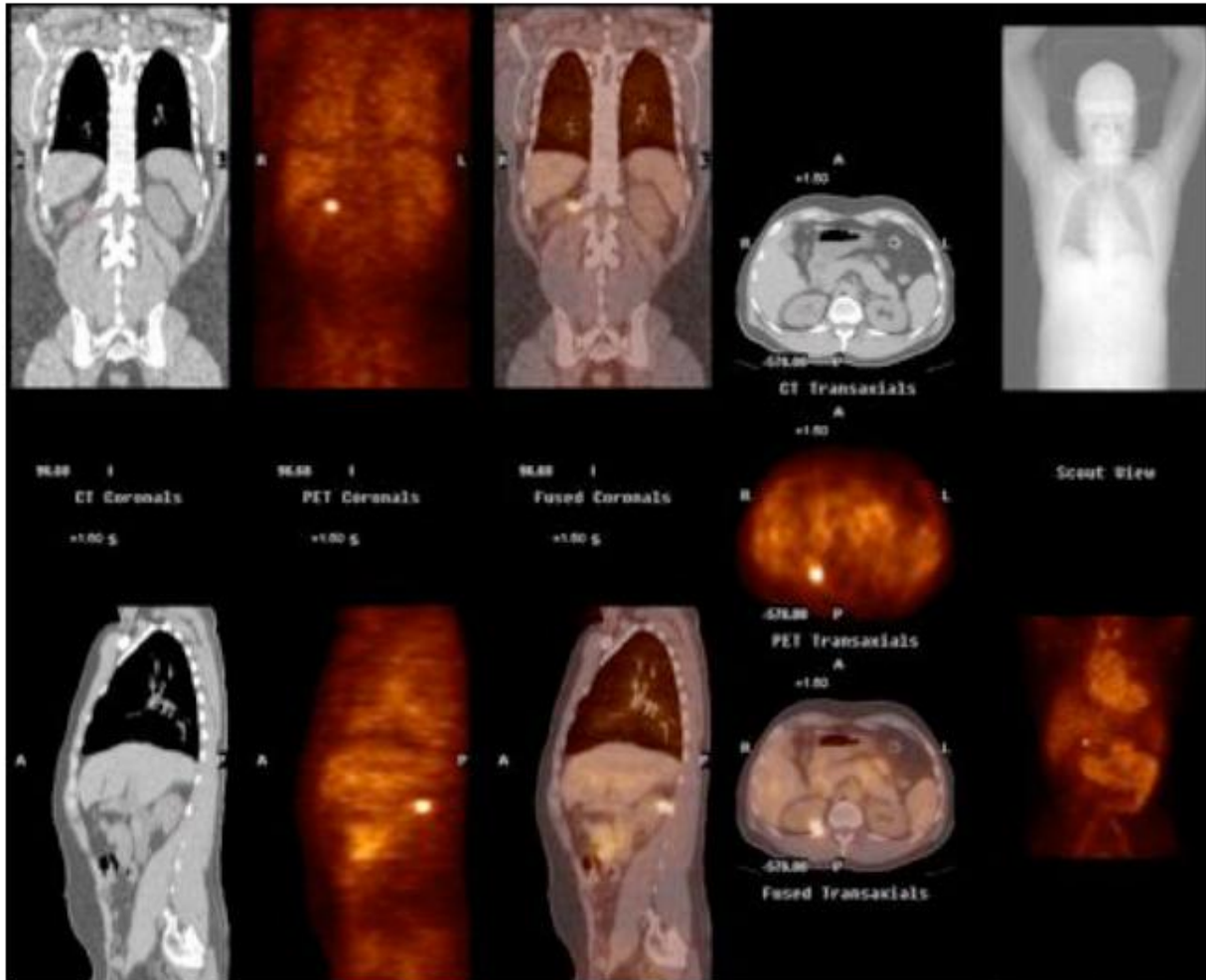
Primary tumour left kidney

Rib metastasis

Clavicle metastasis

Courtesy of Michael Yu,
Fox Chase Cancer Center

REDECTANE^(R) detects also small tumours: T1a (1.7cm) ccRCC



Courtesy of Michael Yu, Fox Chase Cancer Center

- **Final data published in May 2010: REDECTANE® outperformed CT**

- **REDECTANE® in comparison to CT**
 - Specificity: confirmed with a highly statistical value $p < 0.001$
 - Sensitivity: also achieved statistical significance with $p \leq 0.016$

- **REDECTANE® in comparison to an arbitrary value of 75% for specificity and sensitivity**
 - Specificity of 87% (95% CI 75-95%) ($p = 0.057$)
 - Sensitivity of 86% (95% CI 79-91%) ($p \leq 0.002$)

- **To avoid unnecessary surgery, high specificity is required (ccRCC is not present)**



In-vitro diagnostic

Univariate analysis of biomarker in trastuzumab-treated MBC

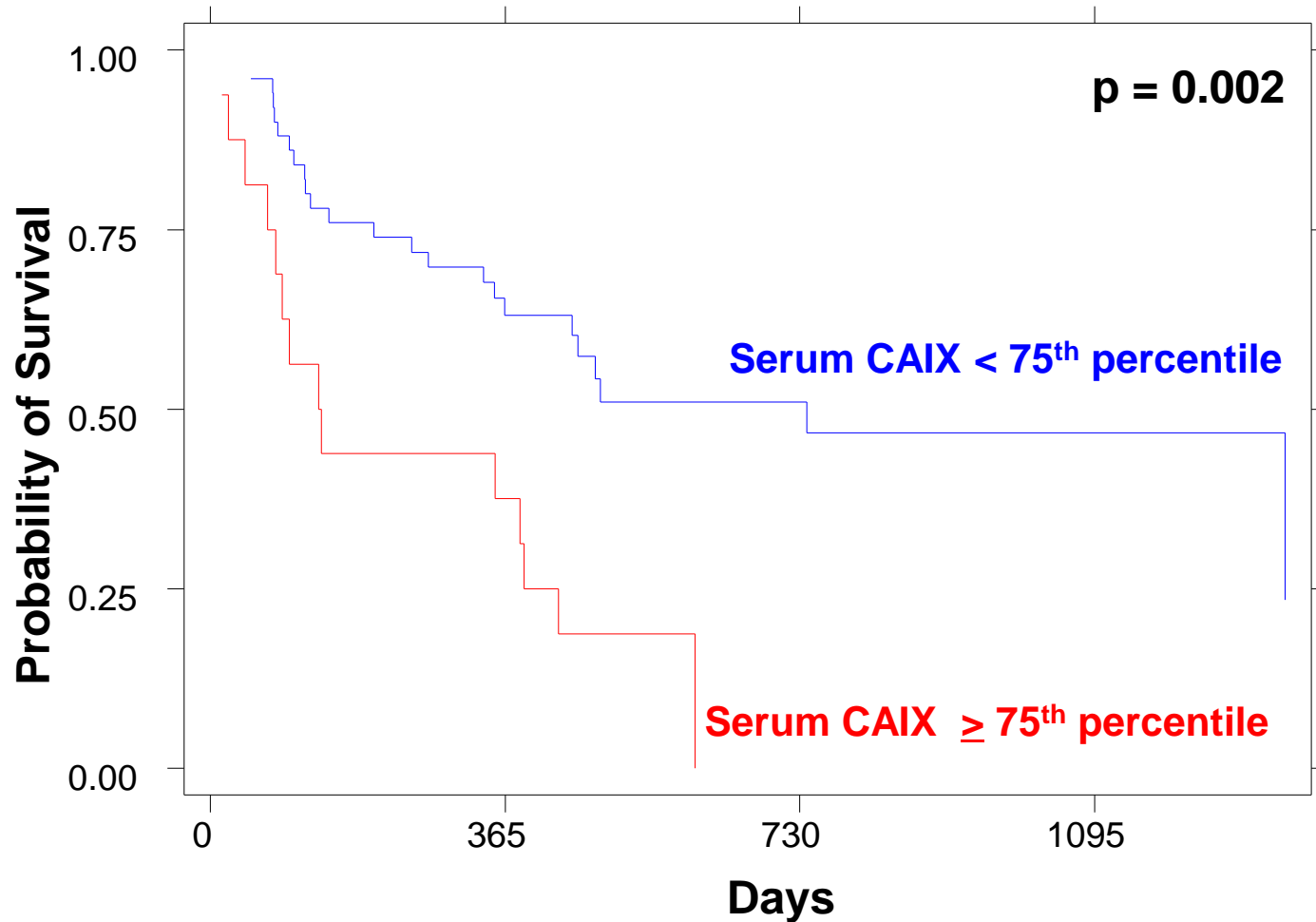
→ **Univariate Analysis:** statistical evaluation of a single variable

Elevated Serum Biomarker	Progression Free Survival (PFS) p-value	Overall Survival (OS) p-value
HER2	0.005	0.018
TIMP-1	<0.0001	<0.0001
uPA	0.006	<0.0001
Endoglin	0.008	0.002
CAIX	<0.0001	<0.0001
VEGF	Ns	Ns

* CAIX=Carbonic Anhydrase 9

Leitzel K, et al. Presented: ASCO 2009 Annual Meeting, Orlando, FL: Abstract # 11092, Board S14, General Poster Session, Mon. June 1, 2009, 1:00PM - 5:00PM, Tumor Biology and Genetics, Level 2, West Hall C

Elevated pretreatment serum CAIX predicts reduced survival



• CAIX=Carbonic Anhydrase 9

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Multivariate Analysis: involves observation and analysis of more than one statistical variable at a time. In design and analysis, the technique is used to perform trade studies across multiple dimensions while taking into account the effects of all variables on the responses of interest.

→ Progression-Free Survival (PFS)

→ Including all 6 biomarkers, only serum CAIX remained a significant independent covariate ($p=0.002$)

→ Overall Survival (OS)

→ Including all 6 biomarkers, only serum CAIX remained a significant independent covariate ($p=0.001$)

→ Conclusions

→ Elevated pretreatment serum CAIX predicted reduced PFS OS in MBC patients treated with first-line trastuzumab-containing therapy

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CAIX: important oncological biomarker in the development of personalised medicine

- **CAIX represents an example of a specifically expressed and tumour associated protein**
 - that can be utilized for further development of personalised therapies and
 - warrants further clinical trials
- **Association between CAIX levels in tumors and patient outcome reported**
- **Significant levels of CAIX protein have been detected in a variety of tumors**
 - e.g. kidney, cervix, lung, bladder, colon and head & neck



Forward looking statements

This communication contains certain forward-looking statements, relating to the Company's business, which can be identified by the use of forward-looking terminology such as "estimates", "believes", "expects", "may", "will", "should", "future", "potential" or similar expressions or by general discussion of strategy, plans or intentions of the Company. Such forward-looking statements involve known and unknown risks, uncertainties and other factors, which may cause our actual results of operations, financial condition, performance, or achievements, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements.

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