

Delivering on the Promise of RNAi Therapeutics



Corporate Update & Interim Results

21 September 2011

Forward-Looking Statements



The statements made in this presentation may contain certain forward-looking comments. Actual events or results may differ from the Company's expectations. In addition to the matters described in the presentation, future actions by the European Agency for Evaluation of Medicinal Products, the U.S. Food and Drug Administration or equivalent regulatory authorities in other countries and results of pending or future clinical trials, as well as other risk factors outlined from time to time in the Company's regulatory filings, may affect actual results achieved by the Company. The Alternative Investment Market (AIM) has not reviewed and does not accept responsibility for the adequacy or accuracy of this presentation.

Today's Message



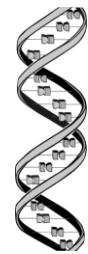
- **Significant changes executed**
- **New leadership with clear business focus**
- **Operations streamlined**
- **Well funded with supportive new investors**
- **Significant scientific and clinical achievements**

PRESENTATION

What is RNAi interference (RNAi)?

“Blueprint For Life”

DNA



Transcription



“Message”

mRNA



**RNA
interference**

Translation



“Body’s Machines”

Protein



Small Molecules
Antibodies

RNAi Therapeutics:

- New class of drugs based on a natural self-defense mechanism
- Recognised by the Nobel Prize to Fire and Mello in 2006
- Virtually all target genes can be addressed subject to functional delivery!
- No need to screen libraries of compounds/antibodies
- Faster pre-clinical development -> faster to market -> earlier revenues

- **World class expertise in RNAi (siRNA) therapeutics**
- **Proprietary novel delivery systems (overcoming the delivery challenge)**
- **One of the industry's broadest siRNA clinical pipelines**
- **Strong validation through pharma and biotech partnerships**
- **Strengthened leadership and commercial focus**

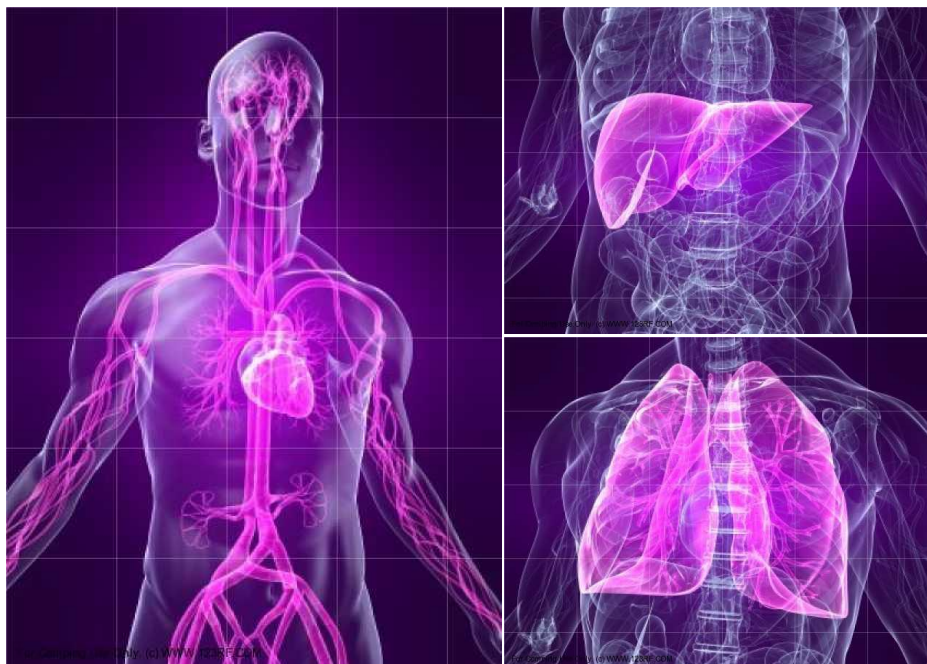
- **Proprietary siRNA (“AtuRNAi”) platform**
- **Five of 13 ongoing clinical siRNA programs worldwide use AtuRNAi**
- **Four Phase II clinical programs ongoing with partners Pfizer/Quark and Novartis/Quark**
- **Over 300 patients exposed to AtuRNAi**
- **Issued patents in US and Europe**

Different lipid delivery technologies target different organ types

AtuPLEX

Vascular endothelium

- Cancer
- Inflammation



DBTC (liver delivery)

Liver parenchyma

- Hepatocellular Carcinoma
- Ischemia Reperfusion Injury
- Fulminant Fibrosis

DACC (lung delivery)

Pulmonary endothelium

- Acute lung injury/ARDS
- Pulmonary Hypertension
- Infection & Inflammation

Silence Product Pipeline



	Products	Indications	Partners	Target	Delivery	Pre-Clinical	Phase I	Phase II	Target Tissue / Organ
Partnered programs	PF-4523655 (AtuRNAi)	Diabetic Macular Edema	Pfizer/Quark	RTP801	Naked siRNA	[Orange bar spanning Pre-Clinical, Phase I, and Phase II]			Local Delivery to the Eye
	PF-4523655 (AtuRNAi)	Age-related Macular Degeneration	Pfizer/Quark	RTP801	Naked siRNA	[Orange bar spanning Pre-Clinical, Phase I, and Phase II]			Local Delivery to the Eye
	QPI-1002 (AtuRNAi)	Prevention of Delayed Graft Function	Novartis/Quark	P53	Naked siRNA	[Orange bar spanning Pre-Clinical and Phase I]			Systemic Delivery to the Kidney
	QPI-1002 (AtuRNAi)	Acute Kidney Injury	Novartis/Quark	P53	Naked siRNA	[Orange bar spanning Pre-Clinical and Phase I]			Systemic Delivery to the Kidney
Internal programs	Atu027 (AtuRNAi)	Solid Tumors	Internal	PKN3	AtuPLEX	[Yellow bar spanning Pre-Clinical and Phase I]			Systemic Delivery to Tumor Endothelium
	Atu134 (AtuRNAi)	Solid Tumors	Internal		AtuPLEX	[Yellow bar in Pre-Clinical]			Systemic Delivery to Tumor Endothelium
	Atu111 (AtuRNAi)	Acute Lung Injury	Internal		DACC	[Yellow bar in Pre-Clinical]			Systemic Delivery to Lung Endothelium
	Atu195 (AtuRNAi)	Solid Tumors	Internal		AtuPLEX	[Yellow bar in Pre-Clinical]			Systemic Delivery to Tumor Endothelium

- **Internal Pipeline**

- **Atu027**

- Atu027 Phase I interim data presented at ASCO in June 2011
 - Enrolment of Cohort 9 of 11 completed
 - Atu027 very well tolerated and encouraging signs of efficacy
 - Effective dose exceeded

- **Atu134**

- Manufacturing of supplies for toxicology studies initiated

- **External pipeline**

- **PF-'655**

- Quark presented encouraging Phase II results of PF-'655 in Diabetic Macular Edema
 - Phase IIb trial to be initiated shortly
 - Phase II trial of PF-'655 in Age-related Macular Degeneration completed

- **QPI-1002**

- Phase II trial of QPI-1002 in Acute Kidney Injury to be initiated shortly
 - Phase II trial of QPI-1002 in Prevention of Delayed Graft Function ongoing

Strong Validation Through Partnerships



- AstraZeneca - \$15M upfront payment with up to \$400M in milestones plus sales royalties for five targets (2007, extended 2010)
- AstraZeneca - Novel approaches to delivery of siRNA molecules (2008, extended 2010)



- Pfizer/Quark - Phase II products for diabetic macular edema and age-related macular degeneration; \$95m milestones plus royalties, \$6m received (2006). Next possible milestone \$4m on start of Phase III trials



- Novartis/Quark - Phase II products for acute renal failure and kidney transplantation; \$82m in milestones plus royalties, \$1m received (2010). Next milestone \$3-11m possible in 2012



- Dainippon Sumitomo - siRNA delivery collaboration, \$2m upfront (2009, expanded 2010)



- InteRNA - microRNA delivery collaboration (2011)

Strategic decision to increase BD resources



More deals generating non-dilutive funding and thereby extending runway

- **New experienced CEO appointed, Thomas Christély**
- **New Chief Business Officer appointed, Tony Sedgwick**
- **Operations centralised in Berlin**
- **Reorganisation of the Group reduces burn rate by £1m p.a.**
- **Reduction in number of non-executive directors**

H1 2011 Financial Highlights











- Revenue £354k (H1 2010: £716k)
- R&D £1.8m (H1 2010: £4.4m)
 - Reorganisation of R&D April 2010 after Intradigm acquisition
- G&A £2.0m (H1 2010: £3.2m)
 - Reorganisation after Intradigm acquisition
 - Includes restructuring cost of £0.4m after closing Redwood City
 - G&A £1.6m excluding one-off restructuring cost
- Raised £5.51m (net of expenses) through placing and open offer in May 2011
- Cash as of 30 June 2011 £6.5m (31 December 2010: £3.6m)
- Cash usage H1 2011: £2.6m

Results for the Six Months ended 30 June



£000s	1H11A ongoing	1H11A restructuring	1H11A reported	2010A
Revenue	354	-	354	2,366
R&D spend	(1,819)	-	(1,819)	(5,821)
Admin costs	(1,560)	(443)	(2,003)	(5,203)
Operating loss	(3,025)	(443)	(2,003)	(8,658)
Other income/(exp.)	42	-	42	(137)
Loss before tax	(2,983)	(443)	(3,426)	(8,795)
Loss after tax	(2,983)	(443)	(3,426)	(8,795)
Net cash			6,486	3,567

~ Funded well into H2 2012 ~

Update on progress of Atu027		Jan. 2011
Update on PF-'655 in diabetic macular oedema (DME)		Mar. 2011
Full year results for 2010		April 2011
Fundraising		May 2011
Present interim Phase I data of Atu027 at ASCO		June 2011
Completion of Phase II trial of PF-'655 in AMD (Pfizer/Quark)		July 2011
Sign new collaborations or extend existing collaborations		Sept. 2011
Further issuance of patents		2H11
Start of Phase IIb trial of PF-'655 in DME (Quark)		2H11
Start of Phase II trial of QPI-1002 in AKI (Quark/Novartis)		2H11
Completion of enrolment in Atu027 trial		1H12

- **RNAi therapeutics will become a major drug class similar in importance to monoclonal antibodies**
- **Silence is one of a few companies well positioned to capitalise on this technology**
- **Changes now fully implemented will drive this forward**

APPENDIX

Atu027 Phase I: Clinical Update

Efficacy

- Stable disease observed in 9 out of 24 patients after treatment phase
- Efficacy and MOA in xenograft models (prostate, breast, lung, colon, pancreatic and other cancers)

PK

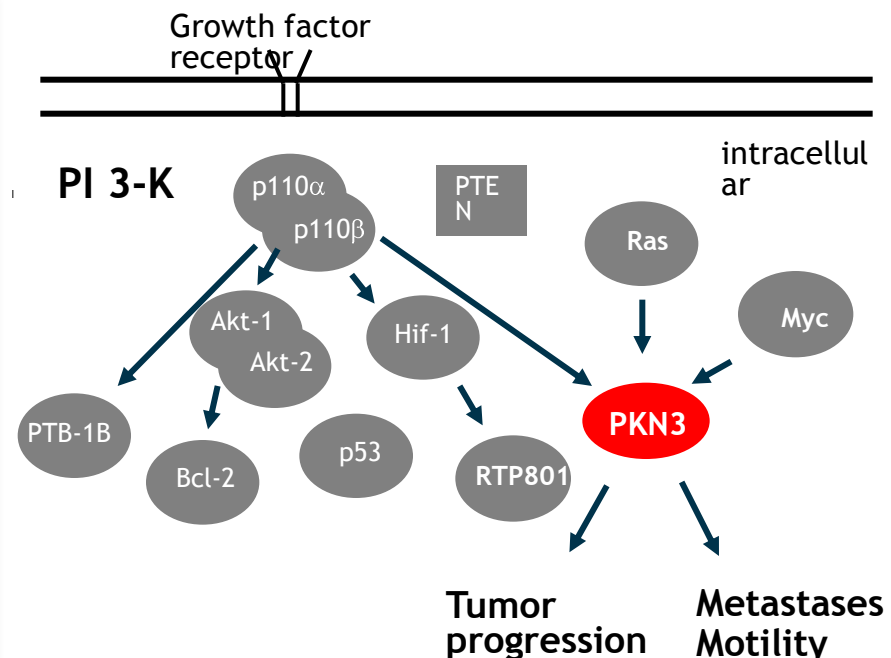
- Dose dependent PK in cynomolgus monkey correlates with PK profile in human

Safety

- No pre-medication with immunosuppressives
- 212 doses administered to 27 patients across 9 dose levels (out of 11 dose levels in total)
- Dose escalation still ongoing
- No dose limiting toxicities so far
- No dose-dependent trends in lab or clinical adverse effects
- 33 doses given to 1 patient incl. compassionate use

CMC

- Lyophilized formulation (shelve life >3 years)



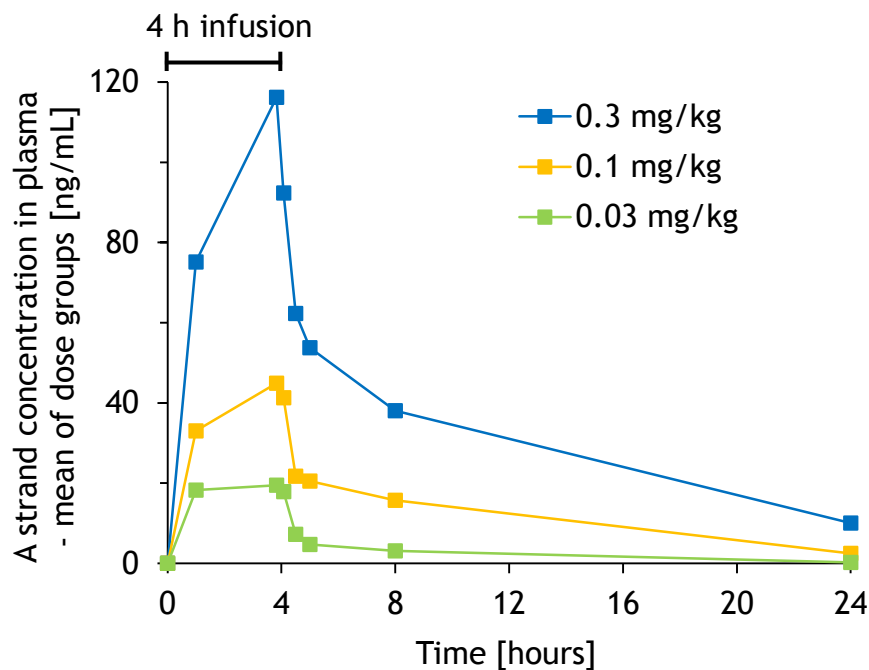
PKN3 plays an important role in angiogenesis and cell motility, major processes leading to metastasis.

Inhibition of PKN3 leads to:

- reduced oxygen supply to tumour
- reduced tumour growth/metastases

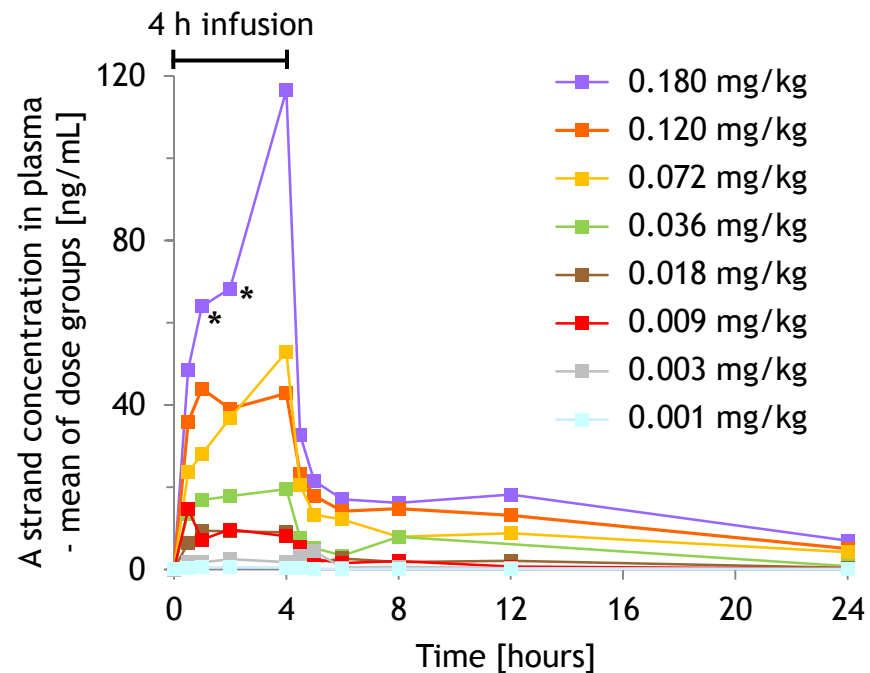
Atu027: Predictable Pharmacokinetics

Cynomolgus Monkey



In vitro: $IC_{50} \approx 1$ to 10 nM

Human

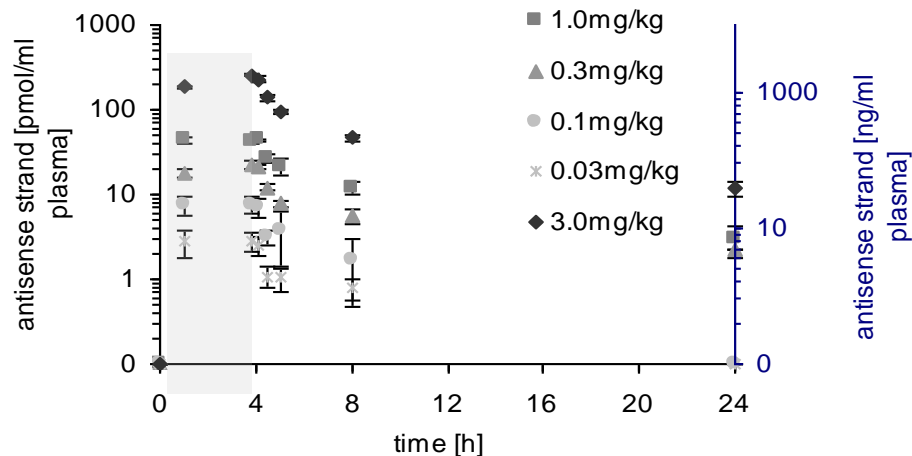


* Final/verified data pending

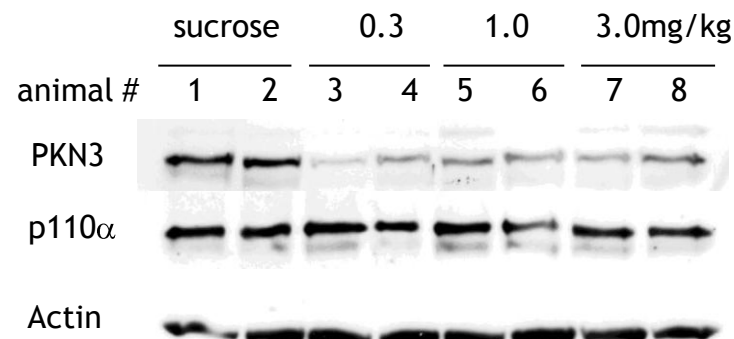
Predictable PK tells that Atu027 is behaving in humans as it did in pre-clinical models

Atu027: Gene knock-down of PKN3 confirmed in preclinical studies

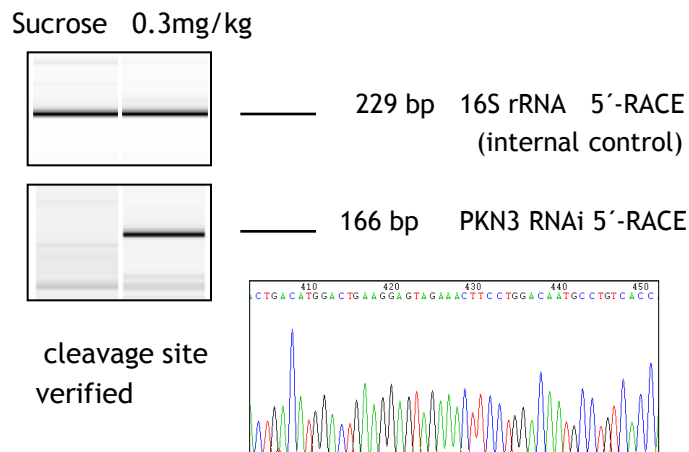
Plasma level of siRNA strand (1st infusion)



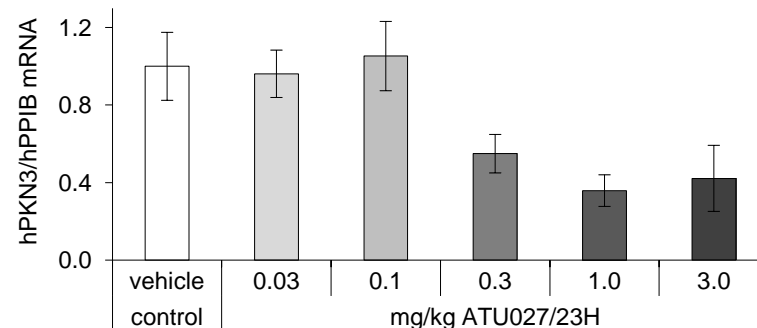
Protein knock down in lung tissue (Western blot)



RNAi in lung tissue (5'-RACE)



mRNA knock down in lung tissue (B-DNA)



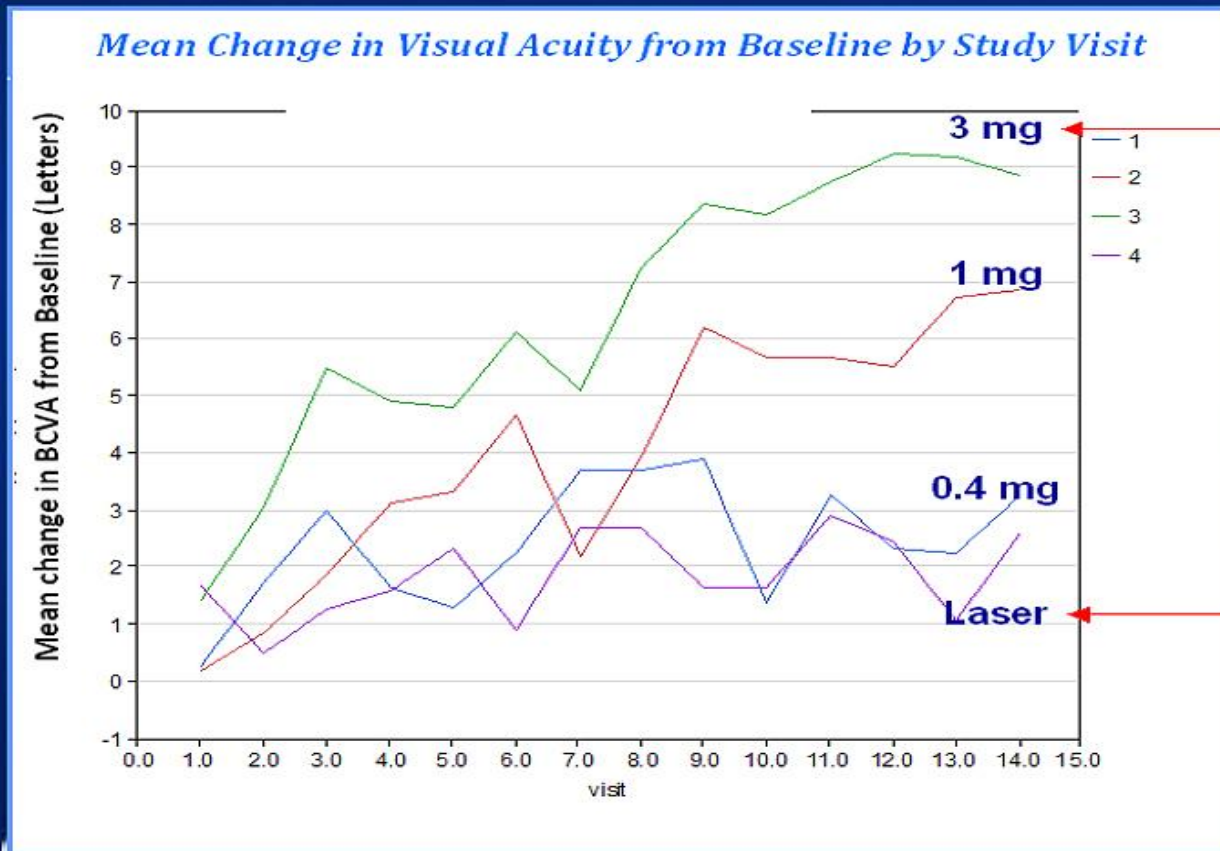
Atu134: Preclinical Plans on Track



- Atu134 has demonstrated efficacy in a variety of preclinical cancer models
 - Orthotopic models
 - Ectopic models
- Atu134 has demonstrated strong efficacy against primary tumour
- Targets CD31 - well validated target
- GMP manufacturing initiated
- Preclinical toxicology testing due to start early in 2012
- IMPD filing expected in 2012

- Quark announced Phase II results in Diabetic Macular Edema in March 2012
 - Demonstrated improved vision at 12 months vs laser therapy
 - Clear dose response observed
 - Maximum tolerated dose not reached
- Quark initiating a Phase IIb trial in Diabetic Macular Edema
 - Pfizer maintains interest but will not fund study
- Phase II results in Age-related Macular Degeneration expected before year-end
- Total milestones to Silence of \$95m
 - \$6m received to date
 - Next milestone c.\$4m on start of phase III trials

Results of Quark Pharmaceuticals Product PF-655 in Patients That Have Completed 12 Months of Treatment and Follow up



Other Clinical Programs - QPI-1002



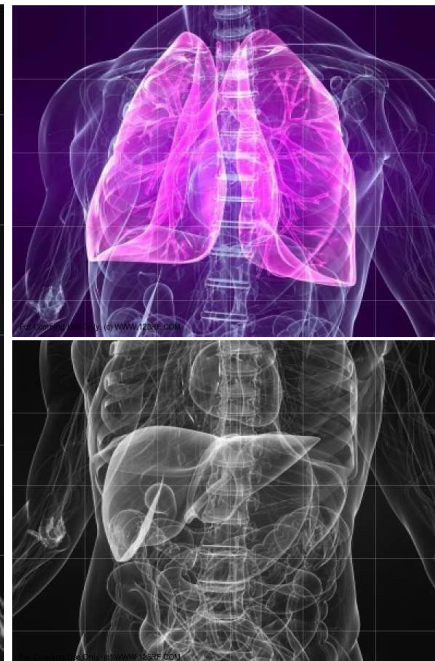
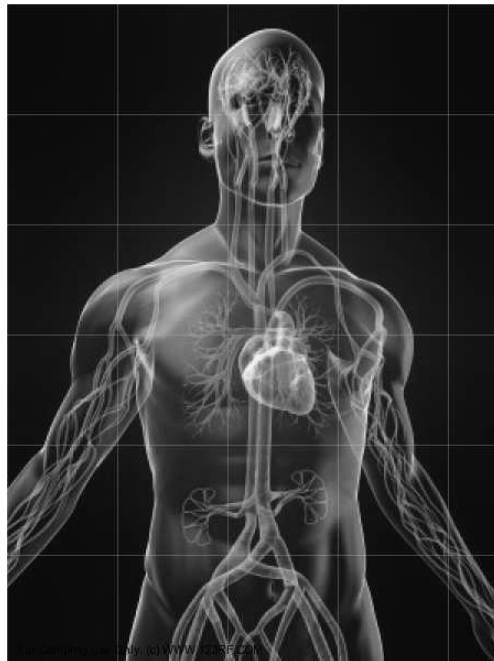
- Prophylaxis of Delayed Graft Function
 - Quark initiated Phase II trial in September 2011
 - Recruitment progressing well
 - Trial expected to complete in H1 2012
- Acute Kidney Injury
 - Phase II trial commencing
- Total milestones to Silence of \$82m
 - \$1m received to date
 - Next milestone c.\$3-11m, if Novartis exercises option

DACC: Focused Delivery to the Lung

AtuPLEX

Validated broad delivery
to vascular endothelium

- Tumor & Metastasis
- Inflammation



DACC

Highly focused delivery to
lung endothelium

- Acute lung injury/ARDS
- Pulmonary Hypertension
- Infection & Inflammation

DBTC

Highly focused delivery to
liver parenchyma

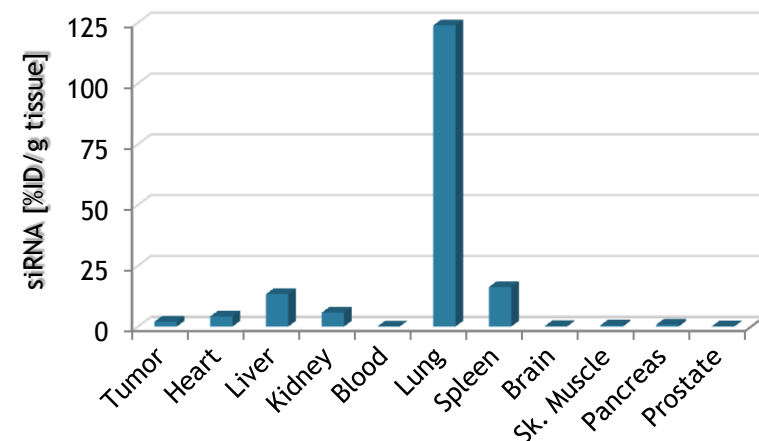
- Hepatocellular carcinoma
- Ischemia Reperfusion Injury
- Fulminant Fibrosis

DACC: Acute Lung Injury and Other Lung Diseases

- Acute lung injury (ALI) is an area of high unmet medical need
- Significant market opportunity:
 - Pneumonia is 2nd highest cause of hospital admissions
 - Pneumonia treatment costs \$8bn/yr in US alone (mortality rate 12-30%)
 - ALI principle cause of mortality
- Other potential applications:
 - Pulmonary Hypertension
 - Infection & Inflammation
- DACC delivery system provides highly focused delivery to lung (see chart)
- DACC delivery system leads to prolonged knock-down - more than 3 weeks
 - potential for only one dose in ALI
- Aim to partner in 2012
 - target single digit royalty rate

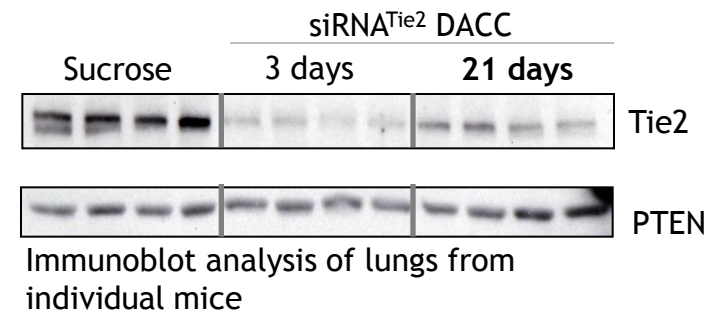
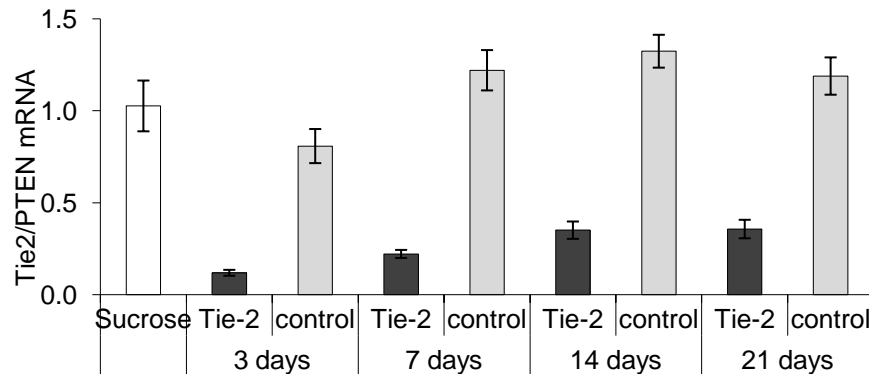


Organ distribution after delivery of siRNA with DACC

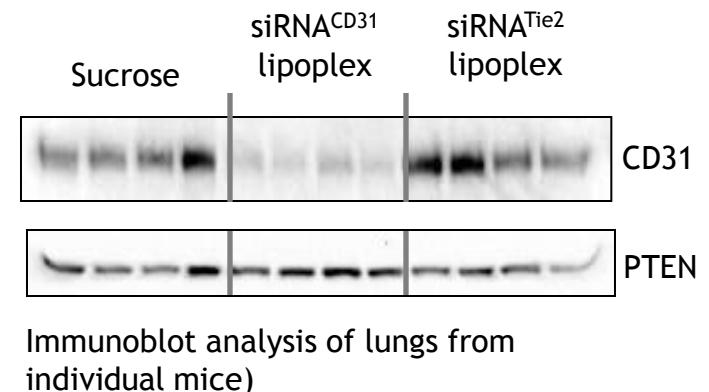
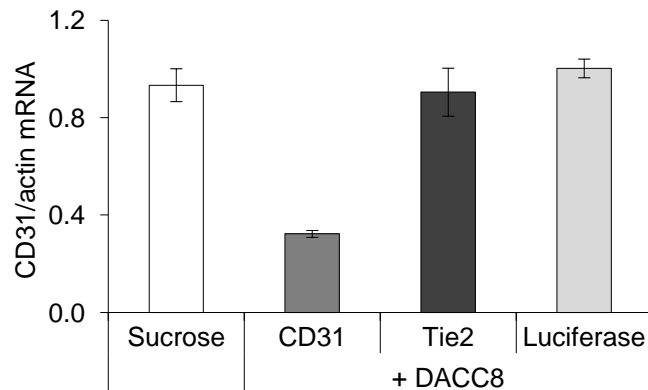


DACC: Long-Term Duration of mRNA and Protein Knockdown (> 21 Days)

Tie-2 mRNA knock-down after 1 single application with DACC



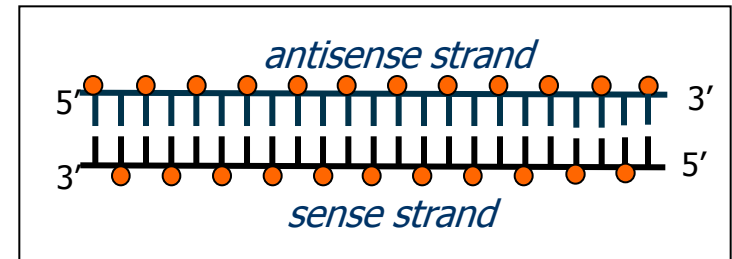
CD31 mRNA knock-down after 1 single application with DACC



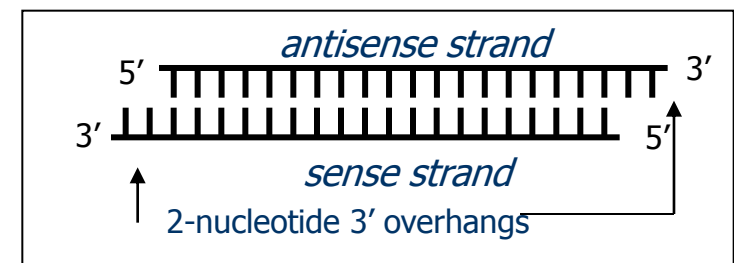
AtuRNAi: The De-Facto Standard

- 2'-O-Methylation offers greater stability and better tolerability
 - Licensed to Pfizer, Novartis and AstraZeneca
 - Further advanced in development than any other RNAi (PF-'655 for DME)
 - Improved stability compared to convent. siRNA
 - No evidence of cytokine stimulation, activation of Toll-Like Receptors or toxic metabolites
 - Over 300 patients treated to date
- Blunt-end strands show equivalent knock-down to overhangs
- Faster preclinical development
 - Same scale up process for all AtuRNAi products
 - Faster regulatory process expected as tox profile for AtuRNAi is known
 - Screening starts directly with modified siRNA
- Lower Cost of Goods
- Issued patents in Europe and US

Silence's AtuRNAi



Conventional siRNA



- Collaboration to deliver novel microRNAs against cancer
- InteRNA gains access to AtuPLEX™ for microRNAs
- InteRNA provides multiple microRNA drug candidates
- Silence receives
 - upfront payment
 - staged payments
- Agreement further confirms AtuPLEX's value beyond delivery of siRNA



Delivering on the Promise of RNAi Therapeutics



Thank you