

CRYSTALGENOMICS, INC.

May 2019



Vision

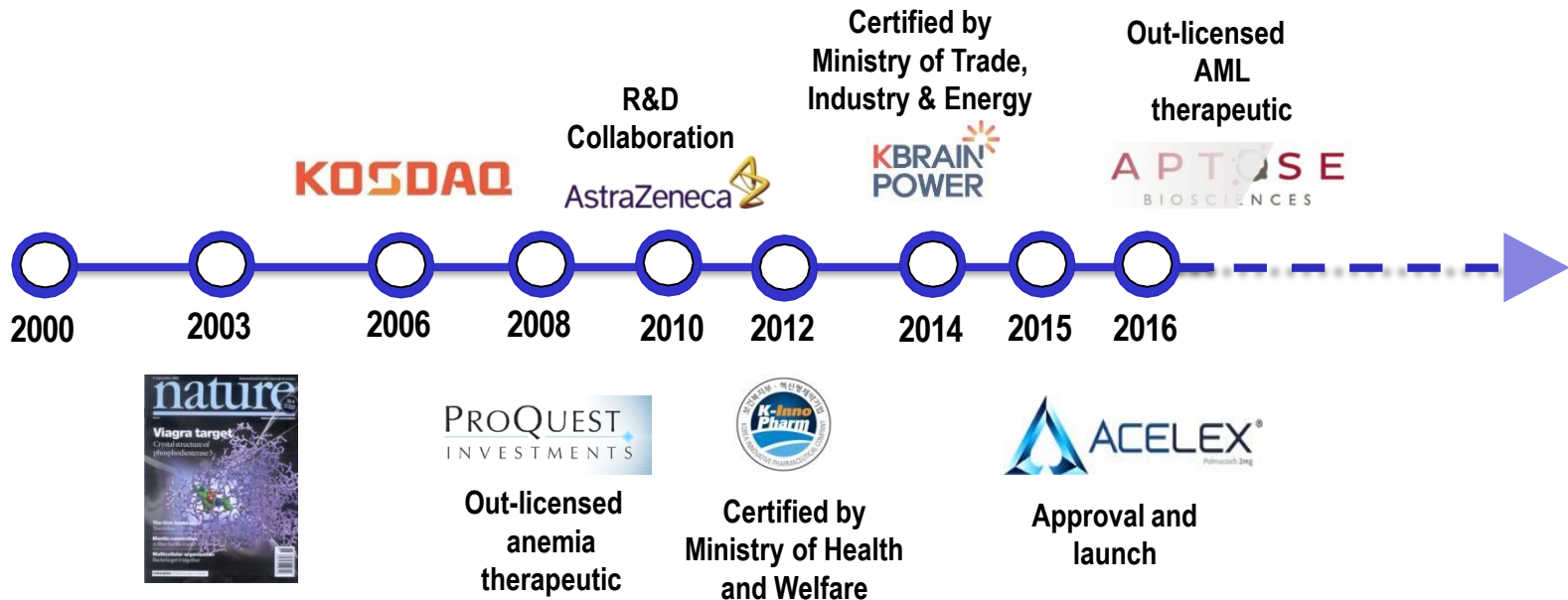
To become a fully integrated global biopharmaceutical company by extending our footprint in Korea and throughout the world



Ticker Symbol: CRYSTAL [083790] – KOSDAQ

Closing Price	KRW 19,850 (March 6, 2019)
52-Week High	KRW 29,220
52-Week Low	KRW 15,650
Market Cap	KRW 801,898,989,900 (~USD 711 Million)

About CrystalGenomics





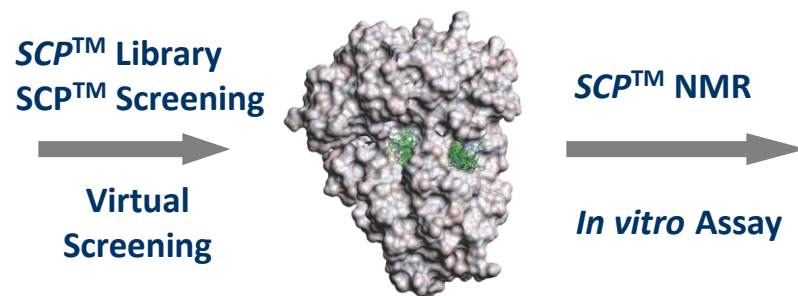
- Possesses competitive drug discovery platform which lead to Korea's first cover page on *Nature*, first time ever by any Korean group, both industry and academia combined
- 1st biotechnology company to IPO on the KOSDAQ exchange under the government's special policy, exempting certain financial criterion for companies with innovative technologies
- 1st Korean biotech to independently accomplish successful development, approval, commercialization, and export of an innovative drug, Acelex[®]
- Biotech that continuously discovers novel drug candidates through its drug discovery platform technologies

CG Discovery Process and Platform Technology

Structure Determination (*SPS*TM)



Lead Discovery (*SCP*TM)

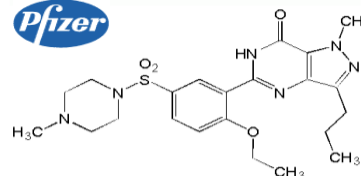


Lead Optimization and Candidate Selection (*SDF*TM)

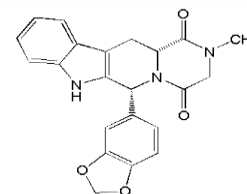




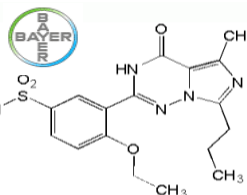
Phosphodiesterase 5 inhibitors



Viagra[®]
(sildenafil)



Cialis[®]
(tadalafil)



Levitra[®]
(vardenafil)

Nature 425, 98-102 (2003).



1. Management Team with Experience and Track Record

- Execution of 4 out-licensing deals with multi-national pharmas involving novel drugs
- NDA submission to the US FDA with multi-national pharma
- 2 R&D collaborations with multi-national pharmas
- Establishment and management of a JV company with a US-based VC

2. Establishment of a Competitive Discovery Platform

- Highly competent research team (21 Ph.Ds)
- Discovery platform related publications on highly prestigious scientific journals (*Nature, EMBO, etc.*)

3. Strengthening R&D through Open Innovation

- Collaborations with domestic and international research organizations
- Strategic alliances with various pharma/biotechs from Japan and US

CG Alliance Partners: Past and Current



Korea Innovative Pharmaceutical Company Designation

- CrystalGenomics was selected by the Korean Government as one of the 'Korea Innovative Pharmaceutical Company' (KIPC) on June 18, 2012.
- KIPC is part of a recent initiative rolled out by the Korean Government where it pledged to nurture and support selected pharma and biotech companies to help them grow into global pharmaceutical companies by 2020.
- CrystalGenomics ranked within the top 10 among all 43 KIPC designated companies.
- Some of the key benefits includes:
 - Favorable pricing & reimbursement benefits for novel drugs
 - R&D and Financial support in research grants, government subsidies, tax breaks, loans, etc.



Product and R&D Pipeline



R&D PIPELINE

Program	Therapeutic Area	Indication	Pre-Clinical	Phase 1	Phase 2	Phase 3
CG-745 IV ⁽²⁾	Oncology	Pancreatic cancer	[Progress bar spanning Pre-Clinical, Phase 1, and Phase 2]			
CG-745 IV ⁽²⁾	Oncology	MDS	[Progress bar spanning Pre-Clinical, Phase 1, and Phase 2]			
CG-745 IV ⁽²⁾	Oncology	AML	[Progress bar spanning Pre-Clinical and Phase 1]			
CG-745 + PD-1 Inhibitor	Oncology	HCC ⁽¹⁾	[Progress bar spanning Pre-Clinical and Phase 1]			
CG-806 ⁽¹⁾	Oncology	AML, CLL, DLBCL	[Progress bar spanning Pre-Clinical and Phase 1]			
Polmacoxib/Tramadol FDC ⁽²⁾	Pain/Inflammation	Acute/Chronic	[Progress bar spanning Pre-Clinical, Phase 1, and Phase 2]			
Polmacoxib/Pregabalin FDC ⁽¹⁾	Pain/Inflammation	Acute/Chronic	[Progress bar spanning Pre-Clinical and Phase 1]			
CG-598 ⁽²⁾	Inflammation	IBD	[Progress bar spanning Pre-Clinical]			
CG-549 ⁽¹⁾	Infectious Disease	MRSA, ABSSSI	[Progress bar spanning Pre-Clinical, Phase 1, and Phase 2]			
CG-750 CAP ⁽²⁾	Fibrosis	IPF	[Progress bar spanning Pre-Clinical and Phase 1]			



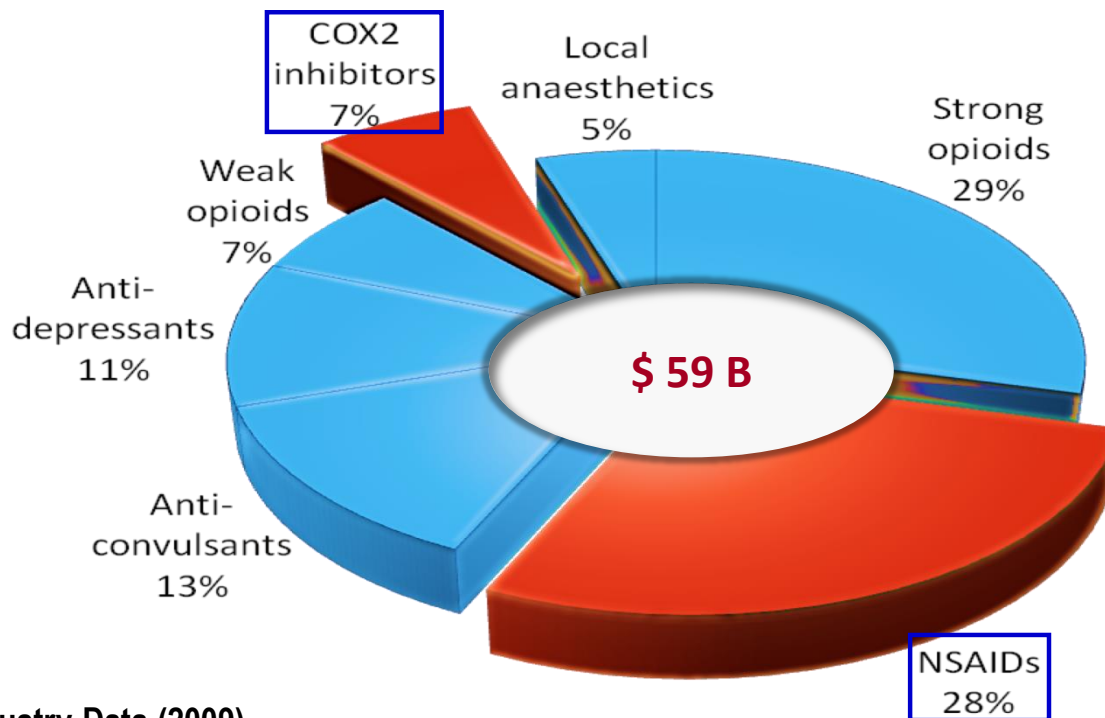
(1) First-in-class, (2) Best-in-class

Acelex[®] (polmacoxib)

Acelex[®]: Growth in Pain Therapeutics Market

- Pain therapeutics market growing due to aging of population and obesity epidemic
- Global market size value estimated at **\$50B** (2011)¹ → **\$59 B** (2015)
- Size of the Nonsteroidal Anti-inflammatory Drugs (NSAIDs) market, including COX-2 inhibitors, approx. **\$ 17.5B**

Global Pain Market



¹IMS Top Line Industry Data (2009)

Acelex[®]: Tissue-Selective COX-2 Inhibitor



Classification	Characteristics	Efficacy	Gastrointestinal Risk	Cardiovascular Risk
Traditional NSAID	<ul style="list-style-type: none"> Aleve (naproxen), Advil (ibuprofen), Voltaren (diclofenac) COX-1 and COX-2 inhibition Dose: > 1000mg/day TID or QID Proton pump inhibitor combination 	Moderate ~ High	High	*Low
Selective COX-2 Inhibitors	<ul style="list-style-type: none"> Celebrex (celecoxib), Arcoxia (etoricoxib) COX-2 selective inhibition Dose: 30~120 mg/day (Arcoxia, Merck) 200 -800mg/day (Celebrex, Pfizer) 	Moderate ~ High	Low	*Low
Tissue-Selective COX-2 Inhibitor	<ul style="list-style-type: none"> Acelex[®] (polmacoxib) Tissue-selective COX-2 inhibitor Dose: 2mg once a day 	High	Low	**Very low

* Occurrences are rare enough to be considered insignificant

**Acelex[®] has a mechanism of action that potentially allows reduction of cardiovascular risk

Acelex®: Tissue Selective NSAID for Osteoarthritis (OA)

Acelex® 2mg Capsule

Tissue-selective COX-2 inhibitor for relief of pain symptoms of OA

- Approved by the MFDS* (Feb. 2015),
- Launched in Korea by Dong-A ST (Sep. 2015)
- Additional commercial partnering with Daewoong (Mar. 2018)
- Second biggest selling COX-2 inhibitor
(behind Pfizer's Celebrex but ahead of Merck's Arcoxia)
- Partnered with TR-Pharm for Turkey & MENA (Jan. 2016)
- Partnered with APSEN for Brazil (Sep. 2018)
- Partnered with PharmArtis International for Russia (Nov. 2018)



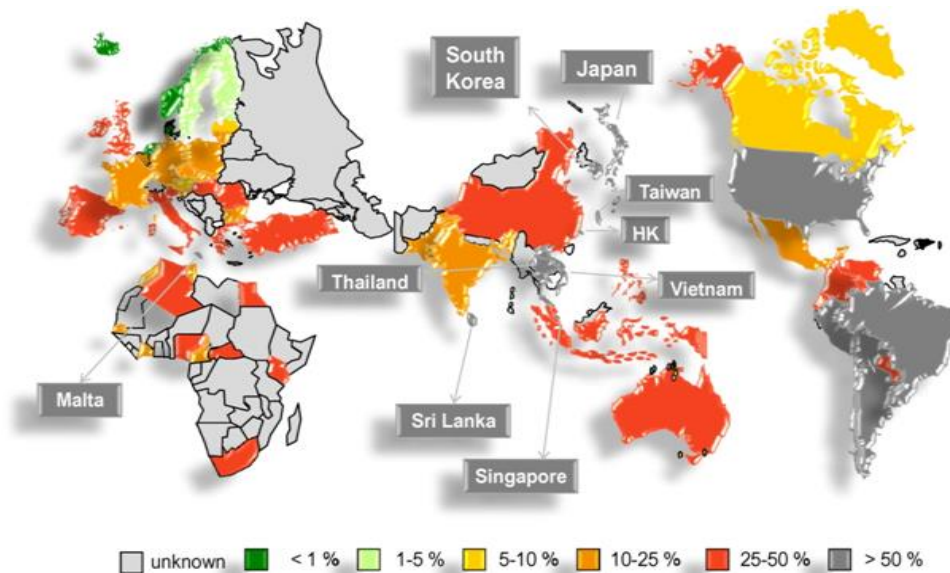
Category	Advantages of Acelex
Efficacy	<ul style="list-style-type: none"> • Quicker onset of relief from the signs and symptoms of OA over Celebrex • Superior PGA (Physicians Global Assessment) scores compared to Celebrex
Dosage	<ul style="list-style-type: none"> • Lowest daily dose among all known NSAIDs • Once-a-day dosing regimen unlike most traditional NSAIDs
Gastrointestinal Safety	<ul style="list-style-type: none"> • Better gastrointestinal (GI) safety in comparison to traditional NSAIDs
Cardiovascular Safety	<ul style="list-style-type: none"> • Cardiovascular (CV) safety to potentially minimize CV side effects

*MFDS: Ministry of Food and Drug Safety of Korea

CG-549: Novel Antibiotic

CG-549: MRSA is a Global Epidemic

- Methicillin Resistant *Staphylococcus aureus* (MRSA) is often referred to as the “Super Bug”
- President Obama issued an executive order in 2014 to combat antibiotic resistance
- According to the CDC, over 72,000 invasive MRSA infections and 9,194 related deaths occurred in 2014
- The global antibiotics market is estimated to be **\$27 billion** of which MRSA market is estimated to be **\$1.4 billion** as of 2014 (GlobalData)
- The standard of care treatments such as vancomycin, linezolid and daptomycin, all have toxicities and usage limitations.

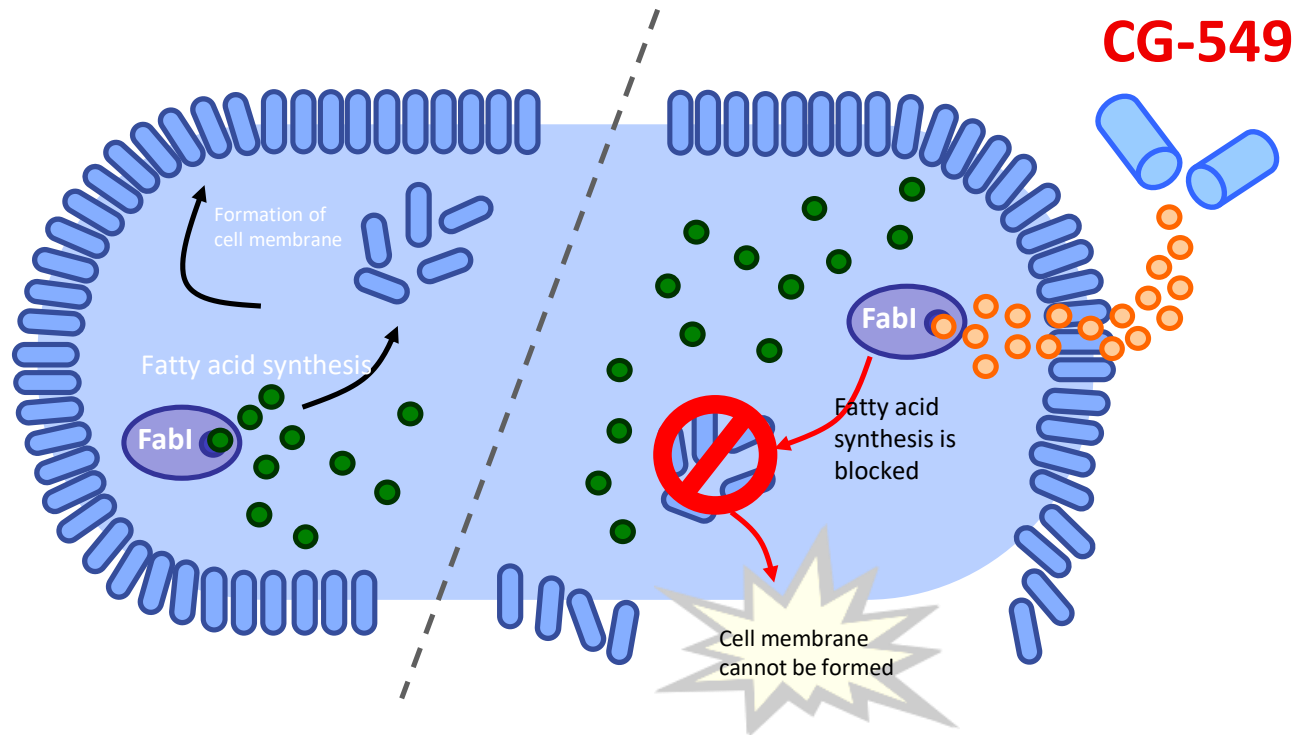


Worldwide prevalence of hospital-acquired MRSA
(Global Epidemiology of MRSA, 2014)

CG-549: First-in-class FabI Inhibitor



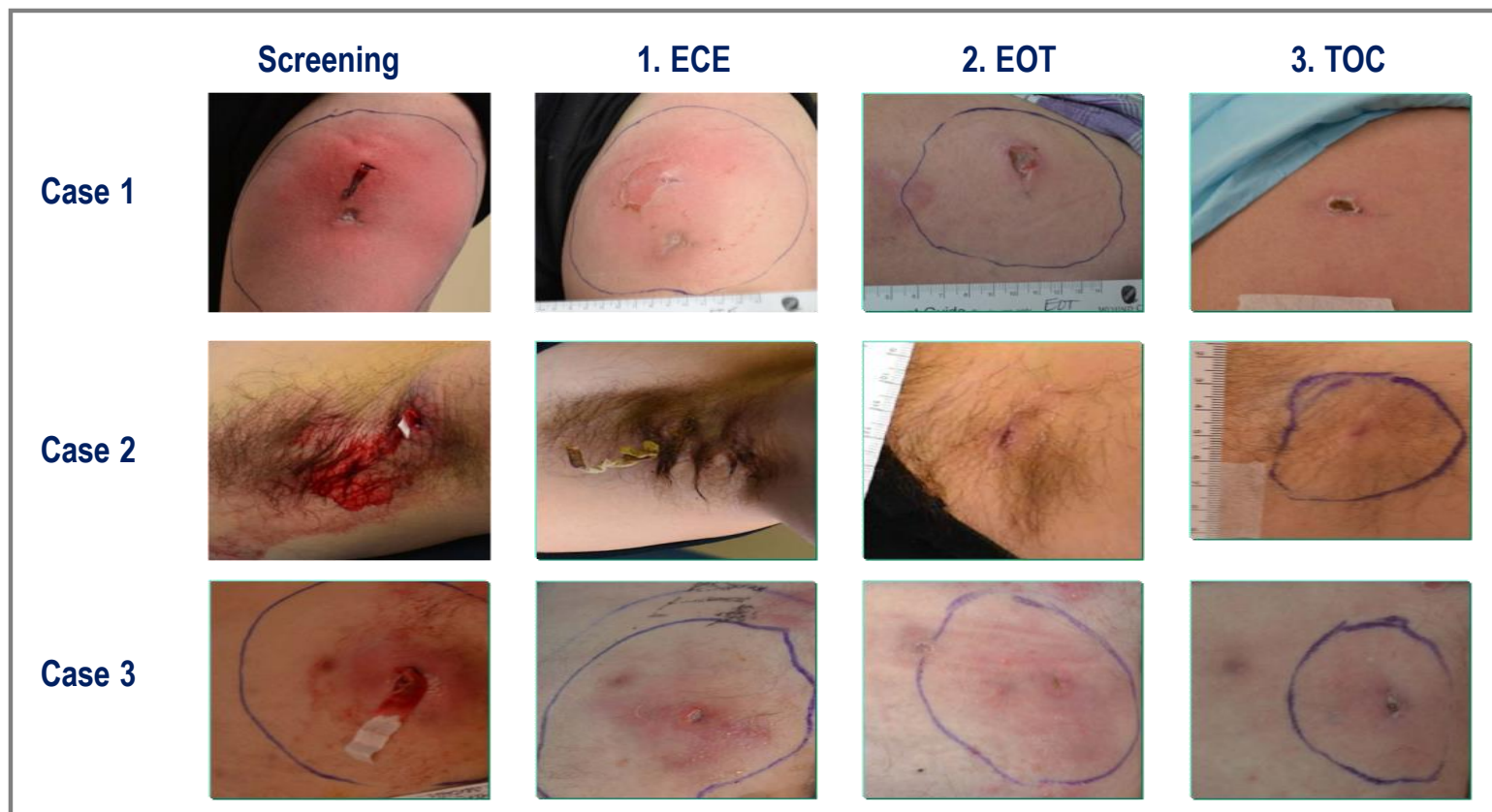
- Fatty-acid biosynthesis inhibitor (FabI)
- Novel mechanism to block a key enzyme in the bacterial cell membrane formation pathway



CG-549: Phase II Conducted in the United States



- Phase IIa study for POC completed in the USA showed 100% of evaluable subjects had been clinically cured by the end of the study
- Formulations for both oral and IV



1. ECE : 48-72 hours after Day 1 2. EOT : 10-14 days after Day 1 3. TOC : 21-28 days after Day 1

CG-549: Less Toxicity Compared to Other MRSA Agents

CG-549 has not shown any of the major toxicities of current therapies.

CG-549 has not shown any of the major toxicities observed in the clinical trials of recommended therapies listed in the guideline of Infectious Disease Society of America (IDSA). As a reference, the NOAEL in the 4 week toxicity studies was 100 mg/kg.

“Clinical Practice Guideline by Infectious Disease Society of America for the Treatment of MRSA Infections in Adults and Children” *Clinical Infectious Diseases* 2011, 38.

Drug		Toxicities Listed in IDSA Guidelines
Vancomycin	IV	- Nephrotoxicity - Hearing loss
Linezolid	IV/ PO	- Hematologic toxicity (thrombocytopenia..) - Irreversible peripheral & optic neuropathy - Lactic acidolysis - Diarrhea, vomiting, loose stools, nausea
Daptomycin	IV	- Elevating CPK - Inducing eosinophilic pneumonia
Clindamycin	PO	- Diarrhea (20% of patients) - <i>Clostridium difficile</i> related diseases
Tetracyclines (Doxycycline, Minocycline, Tigecycline)	IV/ PO	- Increasing all-cause mortality - Decreasing bone growth - Tooth enamel discoloration
TMP-SMX	IV	- Hyperkalemia
Quinupristin-dalfopristin	IV	- Arthralgias, myalgias, nausea, - Infusion-related reactions
Televancin	IV	- Nephrotoxicity
Ceftaroline	IV	- Typical cephalosporin toxicities such as rash, GI troubles (diarrhea..) - 11% of Coombs' test positive (autoimmune hemolytic anemia)

CG-745: Epigenetic Cancer Therapeutic

CG-745: Best-in-class Histone Deacetylase (HDAC) Inhibitor

- CG-745 has a superior pharmacokinetic (PK) and safety profile over other HDAC inhibitors (both approved & in development) due to its high level of drug exposure even at low doses
- Superb efficacy: 56% of all patients had stable disease in the Phase I study, an all-comer study which included a variety of solid tumor patients
- Myelodysplastic syndrome (MDS): Monotherapy / Phase II in progress in Korea
- Pancreatic cancer: Triple combination / Phase II in progress in Korea
- Hepatocellular carcinoma (HCC): CG-745 & APL-501 (PD-1 inhibitor) combination / Global Phase I/II in preparation

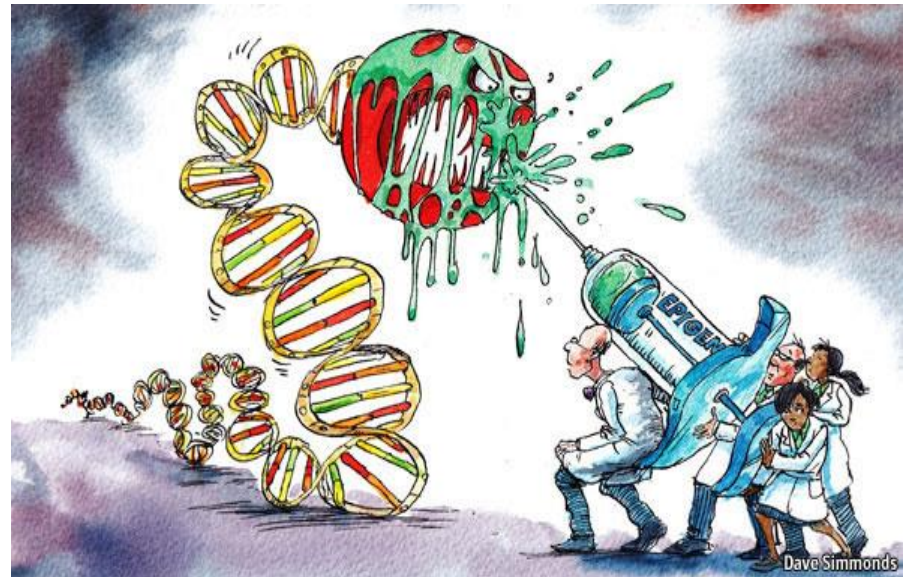
**The
Economist**

Cancer and epigenetics

Cancer's epicentre

New understanding of how cancers work is yielding new treatments

Apr 7th 2012



Clinical Study Design - MDS



A Phase I/II Study of CG200745 (CG-745) PPA to Determine the Maximum Tolerated Dose and Evaluate the Safety and Efficacy in Patients With Myelodysplastic Syndrome (MDS) Who Failed to Respond to Prior Hypomethylating Therapy (ClinicalTrials.gov Identifier: NCT02737462)

Phase Ib

CG-745 Monotherapy

Dose level	CG-745
1	150 mg/m ²
2	225 mg/m ²
3	300 mg/m ²

1. '3+3' dose escalation
2. MTD confirmation
3. Dose selection

Dose Selection



**Selected
225 mg/m²**

Phase II

CG-745 Monotherapy

225 mg/m²

- Once a day for 5 days (Day 1, Day 2, Day 3, Day 4, Day 5), then off Day 6 ~ 28
- IV infusion for 1 hour

**To confirm safety and efficacy
of CG-745 as a monotherapy**

- 1 cycle: 4 weeks
- **Phase Ib completed, Phase II in progress**

Clinical Study Design – Pancreatic Cancer

A Phase I/II Study of Combination Therapy of CG200745 PPA With Gemcitabine and Erlotinib to Determine the Maximum Tolerated Dose (MTD) and Evaluate the Safety and Efficacy for Locally Advanced Unresectable, or Metastatic Pancreatic Cancer (ClinicalTrials.gov Identifier: NCT02737228)

Phase Ib

Gemcitabine 1000 mg/m²
+
Erlotinib 100 mg
+
CG-745 (mg/m²)

Dose level	CG-745
0	125
1	187.5
2	250
3	312.5

Dose Selection



**Selected
250 mg/m²**

Phase II

Gemcitabine 1000 mg/m²

- Once a week for 3 weeks (Day1, Day8, Day15), then 1 week off
- IV infusion for 30 mins

+

Erlotinib 100 mg

- Once daily for 4 weeks, after meal

+

CG-745 250 mg/m²

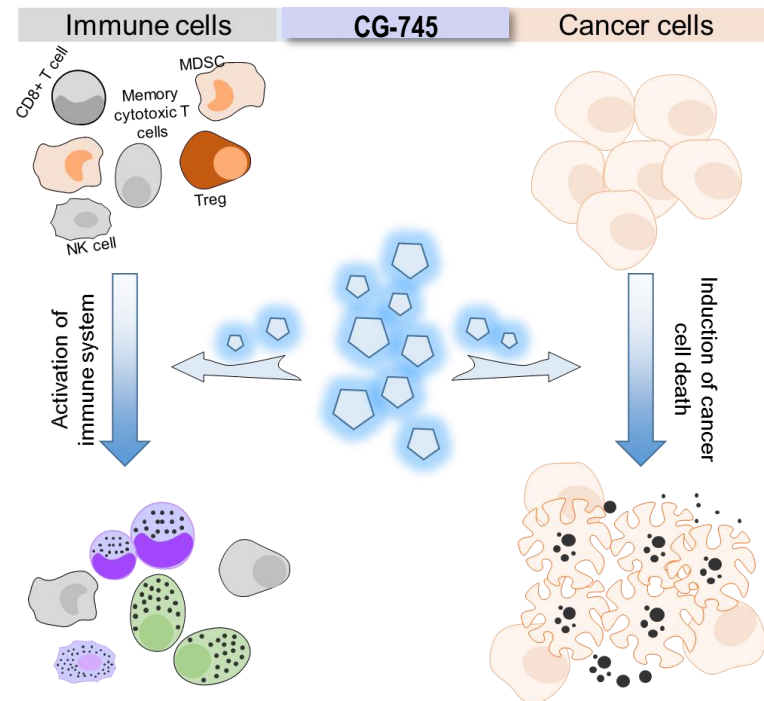
- Once a week for 3 weeks (Day1, Day8, Day15), then 1 week off
- IV infusion for 1 hour

- 1 cycle: 4 weeks
- **Phase Ib completed, Phase II in progress**

CG-745: Immuno-boosting & Direct Anti-cancer Effects

- CG-745 is expected to have an important role in anti-cancer therapy as it has both direct cancer cell killing effect as well as immuno-stimulation effects, making it a superb combination drug of choice for checkpoint inhibitors such as APL-501 (PD-1 inhibitor), especially for solid tumors

- High inhibitory effect on HDACs
- Direct effect on cancer death
- Increases CD4+ and CD8+ T cell proliferation
- Increases killing effects of NK cells
- Increases anticancer cytokine expression
- Downregulation of SETDB1 expression by CG-745 is expected to show good efficacy in liver cancer



Potential Indications of CG-745



Cancers	Cell level	Animal	Clinical
Pancreatic cancer*	<ul style="list-style-type: none"> - Anti-proliferation and cellular mechanism has been studied in various cell lines and in Gemcitabine resistant cell lines - Synergies in anti-cancer activity and cellular signaling were confirmed with co-treatment of standard therapy 	Confirmed the anti-tumor activity and synergistic effects of combination with standard therapy	<ul style="list-style-type: none"> • P II study in progress
MDS*	<ul style="list-style-type: none"> - Anti-proliferation and cellular mechanism has been studied in various cell lines and in Azacitidine and Decitabine resistant cell lines 	Confirmed the anti-tumor activity and synergistic effects of combination with standard therapy	<ul style="list-style-type: none"> • P II study in progress
Colon cancer	<ul style="list-style-type: none"> - Anti-proliferation and cellular mechanism has been studied in the various cell lines 	Confirmed the anti-tumor activity and synergistic effects of combination with standard therapy	≈ 80% SD from P I SAD study
Prostate cancer	<ul style="list-style-type: none"> - Anti-proliferation and cellular mechanism has been studied in the various cell lines 	Confirmed the anti-tumor activity and synergistic effects of combination with standard therapy	-
Biliary cancer	<ul style="list-style-type: none"> - Anti-proliferation and cellular mechanism has been studied in the various cell lines and in Gemcitabine resistant cell lines 	-	-
Liver cancer	<ul style="list-style-type: none"> - Anti-proliferation and cellular mechanism has been studied in the various cell lines - Synergies in the anti-cancer activity and cellular signaling were confirmed with the co-treatment of standard therapy and checkpoint inhibitors 	Confirmed the anti-tumor activity and synergistic effects of combination with PD-1 inhibitors	<ul style="list-style-type: none"> • Global P Ib/II study planned

*Orphan Drug Designation obtained from MFDS; May be eligible for conditional approval(s) following P II study(s)

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