# Chronicles of EGFR TKIs

Erlotinib (Tarceva) & Gefitinib (Iressa) are the first class of drugs as epidermal growth factor receptor (EGFR) kinase inhibitors for non-small cell lung cancer (NSCLC) treatment. However, their clinical use is ultimately limited due to the mechanism-based toxicity and development of drug-resistance EGFR T790M mutation. Osimeritinib (Tagrisso), an irreversible inhibitor, has recently approved as for the next generation treatment option to overcome the short-comings of the first class drug use. Latest Osimeritinib clinical trial report reveals new acquired-resistant mechanism: EGFR C797S mutation limits the irreversible inhibitor.

In this presentation, new medicinal chemistry strategy is discussed to address the currently unmet-medical needs for EGFR-related NSCLC patients. Reversible pyrimidine-based inhibitors and allosteric inhibitros are explored to overcome EGFR L858R/T790M/C797S and EGFR ex19del/T790M/C797S triple mutants for effective clinical treatment for NSCLC patients.

# KWANGHO LEE

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**ACCOMPLISHMENT**

- Discovery of **DRAK2** inhibitor TRD-0257 → licensed out to 메드팩토 (2017)
- Discovery of BBT-401 for **Pellino-1** inhibition → licensed out to BridgeBio Therapeutics Inc. (2015) → *Ph1 study finished*.
- Discovery of BD1-selective **BET** inhibitor → licensed out to 동화약품(2015)
- Discovery of selective **Ack1** inhibitor → licensed out to ㈜인투셀 (2015)
- **Translational Research Institute of Novel Drug (TREND)** Director (미래부 기초연계중개연구 과제책임자)
- Discovery of selective **c-MET** inhibitor → licensed out to 에이비온 (2014)
- **Invertor of Rociletinib (CO-1686)** for Epithermal Growth Factor Receptor (**EGFR**) mutant selective inhibitors (EMSI): Lead fully out-sourced medicinal chemistry program as program team head (chemistry) → licensed to Clovis Oncology for $209M, → terminated after Phase3
- Discovery of **LFF571** a novel Elongation Factor Tu (EFTU) inhibitor → terminated after Phase2
- Discovery of **LBM415** Peptide Deformylase Inhibitors (PDF) → terminated after Phase1

**EXPERIENCE/RESPONSIBILITY**

2012- Current **Korea Research Institute of Chemical Technology**
*Principal Investigator* Drug & Bio Research Division

2011- Current **University of Science & Technology**
Professor (Medicinal Chemistry & Pharmacology)

2012- 2018 **Translational Research Institute of Novel Drug (TREND)**
Director (미래부 기초연계중개연구 과제책임자)

2008- 2011 **Avila Therapeutics** (merged to **Celgene**)
*Program Team Head (Principal Scientist)* Platform study and **Oncology area research**. covalent inhibition on specific ligand binding. Inhibitors of Apoptosis (IAP), Epithermal Growth Factor Receptor (EGFR) Mutant Selective Inhibitors (EMSI), Bruton's Tyrosine Kinase (BTK) inhibitors for RA and Oncology.

2003- 2008 **Novartis Institutes for BioMedical Research, Inc.**
*Research Investigator I - II* **Infectious Disease area research** (Peptide Deformylase Inhibitors (PDF), Undecaprenyl Pyrophosphate Synthase Inhibitors (UPPS), HCV NS3/4A protease inhibitors, *Elongation Factor Tu* inhibitors (EFTU) and *Bacteria Growth Inhibition* (BGI): Phenotypic Antibacterial Screening).

1992-1997 **CJ Co.**, Kyunggi-do, Korea
*Senior Research Associate* Five and a half years pharmaceutical experience in new drug study on antibacterial drugs (2-Oxazolidinones, Quinolones, and Cephalosporines).

**EDUCATION**

**Harvard University**, *Postdoctoral Fellow*, June 2001 - March 2003
*Advisor*: Professor Yoshito Kishi
**The University of Alabama**, *Ph D. Organic Chemistry*, August 1997 - May 2001
*Advisor*: Professor Jin K. Cha
**Seoul National University**, *M.S. Organic Chemistry*, March 1990 - February 1992
*Advisor*: Professor Eun Lee
**Seoul National University**, *B.S. Chemistry*, March 1986 - February 1990