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T H O M S O N S C I E N T I F I C

Investigator Portal

The Translational Research Knowledge base

Jeff Clovis

Thomson Scientific

Jeff.Clovis@thomson.com



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Research Present and Future...

Within the vast realm of the Life Sciences or
%biomedical research+there is today extreme emphasis on
integration of fundamental discovery and its application in clinical
medicine . *translational science-research-medicine.*

In the U.S. this is influenced
tremendously by the impetus
of the NIH Roadmap --
positioning biomedical
research for the future.



OPASI Office of Portfolio Analysis and Strategic Initiatives
National Institutes of Health

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NIH Roadmap FOR MEDICAL RESEARCH

Re-engineering the Clinical Research Enterprise

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TRANSLATIONAL RESEARCH

OVERVIEW

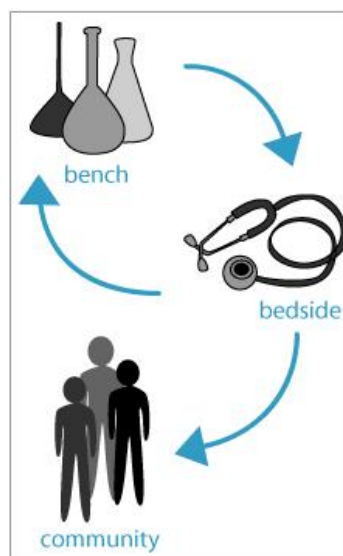
To improve human health, scientific discoveries must be translated into practical applications. Such discoveries typically begin at "the bench" with basic research — in which scientists study disease at a molecular or cellular level — then progress to the clinical level, or the patient's "bedside."

Scientists are increasingly aware that this bench-to-bedside approach to translational research is really a two-way street. Basic scientists provide clinicians with new tools for use in patients and for assessment of their impact, and clinical researchers make novel observations about the nature and progression of disease that often stimulate basic investigations.



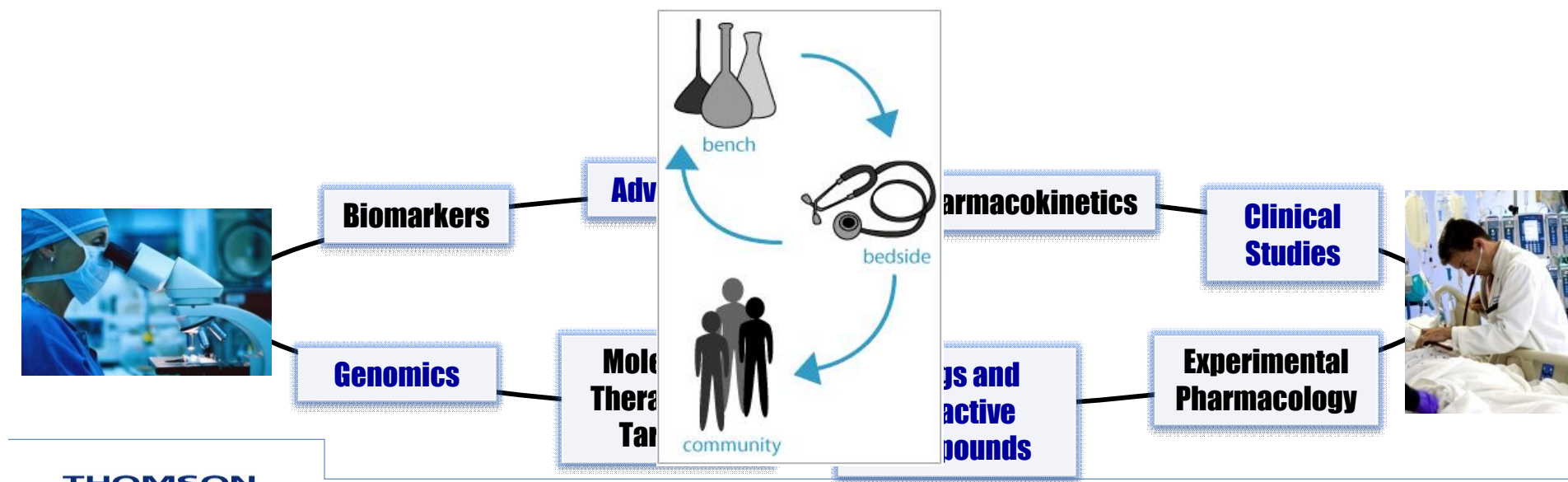
rch sent and Future...

- This collaborative, interdisciplinary approach among traditional researchers and clinicians presents new requirements for supporting informational resources.
- What is needed is a diverse collection of integrated content delivered within a set of tools and features capable of driving fundamental discovery as well as supporting the decision-making process for clinicians and researchers alike.



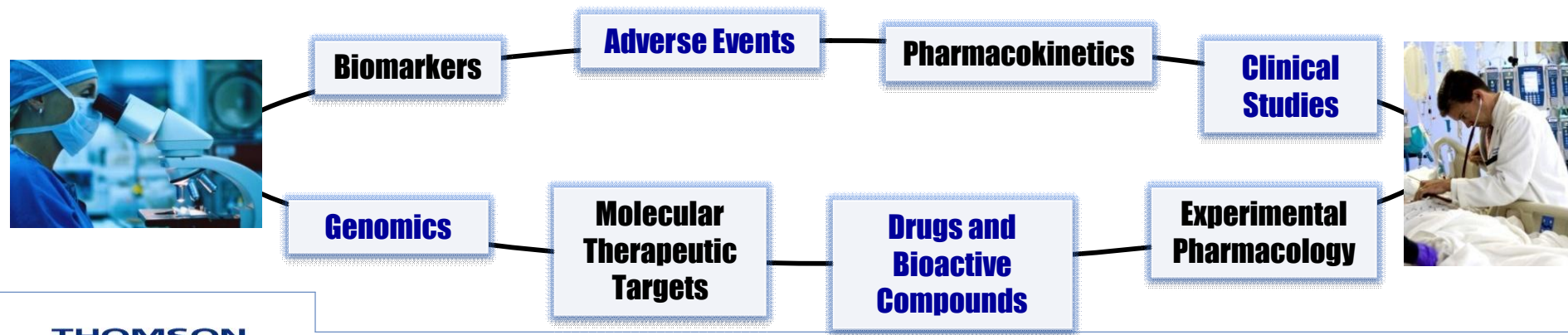
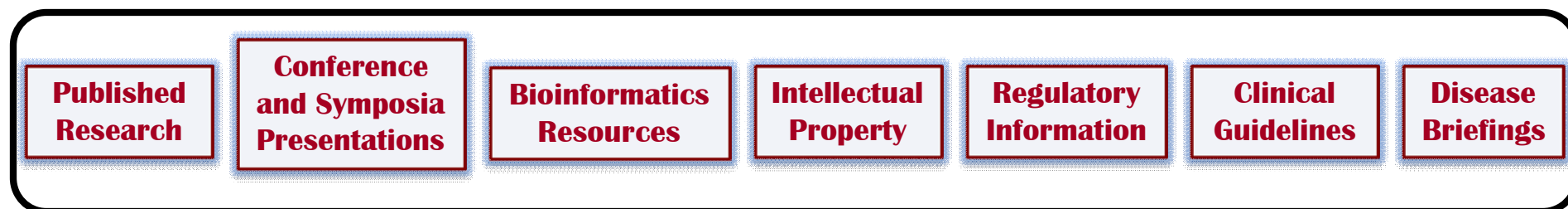
Research Present and Future...

Therefore . Thomson Scientific now presents a diverse collection of *integrated* knowledge-bases in order to serve the molecular biologists, immunologists, pharmacologists, etc. in the lab as well as the oncologists, cardiologists, neurologists, etc. in the clinic.



Research Present and Future...

These knowledge-bases draw from a wide range of sources, are supported by Thomson Scientific experts as well as an international contributor network, and are complemented by additional content such as disease briefings and bioinformatics resources.



Prous Science *Investigator Portal* from *Thomson Scientific* is the resource to optimize workflow in the translational research environment.

It is the source of the vast majority of content we've just presented .

Designed to meet the challenges of interdisciplinary biomedical research.

Quick Search Guided Search

Search Across Knowledge Areas

alzheimer's

Clear Go

From Basic Science to Clinical Research	
Therapeutic Targets & Pathways Molecular structures where drugs interact	176
Drugs & Biologics Therapeutic compounds and procedures	1047
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Congresses	
80th American Heart Association's Scientific Sessions (November 04-07, Orlando, United States) 2007 CITATIONS[248] REPORT	International Congress of the International Psychogeriatric Association (October 14-18, Osaka, Japan) 2007 CITATIONS[21] REPORT
37th Annual Meeting of the Society for Neuroscience (November 03-07, San Diego, United States) 2007 CITATIONS[425]	20th Congress of the European College of Neuropsychopharmacology (ECNP) (October 13-17, Vienna, Austria) 2007 CITATIONS[22] REPORT
11th European AIDS Conference (October 24-27, Madrid, Spain) 2007 CITATIONS[45]	23rd International Conference of Alzheimer's Disease International (October 10-13, Caracas, Venezuela) 2007 CITATIONS[41] REPORT

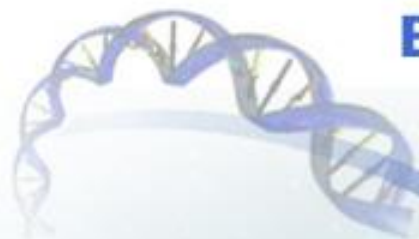
Congresses
7th International Symposium on Ocular Pharmacology and Therapeutics (ISOPT) (February 28-March 02, Budapest, Hungary) 2008 archive
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Biology

- In-depth Understanding of Organizing Biologies: Pathways
- Novel Tools for Target Validation
- Focus on Early Proof of Concept



Chemistry

- Indication Discovery
- Focused Small Molecules Libraries
- Multiple Therapeutic Platforms
- Prediction of Human Drug Metabolism and Toxicity of Novel Compounds



Medicine

Personalized Medicine (Biomarkers & Pharmacogenomics)

- Early Diagnostic
- Selection for Treatment
- Therapeutic Response
- Prognosis

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Sources of Information

“ Patent Offices



11 Patent Offices around the world provide constant updates on product patent status

“ Journals



Over 1,500 journals screened regularly, covering disease and treatment information

“ Scientific Congresses

Over 350 scientific congresses per year covered by medical reporters and writers including official sessions, symposia, poster and oral sessions

“ Company Information

**Press Releases
Annual/Quarterly Reports
Investor Conferences**

“ Regulatory Agencies

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- ⌘ Jeffrey Ross, Cyrus Strong Merrill Professor & Chairman, Albany Medical College, Albany, NY.
- ⌘ Bruce Chabner / Petra Loesch, Director Mass General Hospital Cancer Center, Boston, MA.
- ⌘ Gary Small, Professor Psychiatry & Biobehavioral Sciences/Director UCLA Center Aging
- ⌘ Peter Libby, Professor & Director Cardiovascular Division, Brigham & Women's Hospital, Boston
- ⌘ Richard Jove, Professor & Chair, Division of Molecular Medicine, City of Hope, Duarte, CA.
- ⌘ Eduard Vieta, Prof. Of Psychiatry, Massachusetts General Hospital, Boston
- ⌘ Trevor Hansel, Director, Clinical Studies Unit, NHLI, Imperial College, London
- ⌘ Diederick Grobbee, Professor & Chairman, Julius Center, UMC Utrecht, Netherlands
- ⌘ Satoru Iwase, Vice-Director, Department Palliative Medicine, University Hospital, Tokyo
- ⌘ Hu Dayi, Director Cardiology Department, People's Hospital, Beijing
- ⌘ Keith McGregor, Scientific Director, European Society of Cardiology (ESC)
- ⌘ Matt Peterson, Director of Information, American Diabetes Association (ADA)
- ⌘ J C Kaski, Head Cardiological Sciences, St. George's Hospital Medical School, London
- ⌘ Salvador Peña, Head of Immunogenetics, Free University of Amsterdam
- ⌘ Pere Gascón, Professor & Head of Clinical Oncology, Hospital Clinic, Barcelona

Investigator Portal . The Translational Research Knowledge Base

- “ Vital translational research information solution
 - “ Faster access to structured and relevant information - Increased productivity
 - “ Stimulates hypothesis building - New research lines
 - “ Optimizes workflow - Translational research
- “ Fills unmet need
 - “ First in class unique information resource for translational researchers
 - “ Subscription based business model available by medical specialty
- “ Improvement on current information solutions
 - “ Subscription databases
 - “ Public resources
- “ Designed specifically for academia and government users
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 - ✓ Organized by medical specialties
 - ✓ Analyzed, structured and indexed data

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Areas

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Welcome: **Philip Purnell**

Gateways

- ▶ Gateways to Products
- ▶ Gateways to Patents
- ▶ Gateways to Clinical Trials
- ▶ Gateways to Targets

Today's News

- ▶ Betaferon is only drug to delay disability in patients treated after first MS attack
- ▶ E.U. approves Vectibix for the treatment of metastatic colorectal cancer
- ▶ LifeCycle Pharma initiates phase II clinical trial of immunosuppressant LCP-Tacro
- ▶ OncoVista licenses OSI-7904L from OSI Pharmaceuticals

archive ▶

Dynamic Monographs

Diseases

From Basic Science to Clinical Research

Therapeutic Targets & Pathways

Molecular structures where drugs interact

36

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Genomics

Allelic variants for disease susceptibility and drug- response

Drugs & Biologics

Therapeutic compounds and procedures

1196

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Biomarkers

Indicators of screening, diagnosis, prediction of efficacy & safety as well as monitoring response to treatments

Pharmacokinetics/Metabolism

Kinetic profile of drugs

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Interventional clinical studies in humans

Experimental Pharmacology

Experimental data from drug-receptor and enzyme/target cell interactions

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Innovation discoveries and patents

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Literature
Published references to current literature

9223

Regulatory
Regulatory recommendation for drug R&D

1

Guidelines
Diagnostic, therapeutic and management
guidelines

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Congresses

49th Annual Meeting of the American Society for
Therapeutic Radiology and Oncology (ASTRO)
(October 28-November 01, Los Angeles, United
States) 2007

CITATIONS [5]

AACR-NCI-EORTC International Conference on
Molecular Targets and Cancer Therapeutics
(October 22-26, San Francisco, United States)
2007

CITATIONS [176]

Chest 2007 (October 20-25, Chicago, United
States) 2007

CITATIONS [15]

66th Annual Meeting of the Japanese Cancer
Association (October 03-05, Yokohama, Japan)
2007

CITATIONS [27]

National Cancer Research Institute Cancer
Conference (September 30-October 03,
Birmingham, United Kingdom) 2007

CITATIONS [61]

14th European Cancer Conference (ECCO)
(September 23-27, Barcelona, Spain) 2007

CITATIONS [476]

12th World Conference on Lung Cancer
(September 02-06, Seoul, Korea, Republic of)
2007

CITATIONS [558]

13th International Congress of Immunology
(August 21-25, Rio de Janeiro, Brazil) 2007

CITATIONS [125]

Congresses Found: 220

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Pharmaceuticals

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Dynamic Monographs

Diseases

- ▶ Colorectal Cancer
- ▶ Chronic Obstructive
Pulmonary Disease (Chronic
Bronchitis and Emphysema)

[more](#)

Congresses

- ▶ Annual Meeting of the
American Association of
Pharmaceutical Scientists
(AAPS) (November 11-15,
San Diego, United States)
2007

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Resources

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- Gateways to Clinical Trials
- Gateways to Targets

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- ▶ LifeCycle Pharma initiates phase II clinical trial of immunosuppressant LCP-Tacro
- ▶ OncoVista licenses OSI-7904L from OSI Pharmaceuticals

archive ▶

Dynamic Monographs

Diseases

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Adverse Events

Undesired effects induced by therapy

References

Intellectual Property

Innovation discoveries and patents

578

15462

Literature

Published references to current literature

Click here to see the
list of therapeutic
targets that have been
implicated in this
pathology

Therapeutic Targets and Pathways

Search

26 to 36 records retrieved from 36

1 2

Target Name▼	Type▼	Condition (Status)	Links
<input type="checkbox"/> Mucin 1 (isoform 1)	Protein	Cancer (Validated) Cancer, breast (Validated) Cancer, breast metastatic (Validated) Cancer, colorectal (Candidate) Cancer, kidney (renal cell carcinoma) (Validated) Cancer, lung (Candidate) Cancer, lung (non-small cell) (Validated) Cancer, ovary (Candidate) Cancer, pancreas (Candidate) Cancer, prostate (Validated) Cancer, stomach (Candidate) Lymphoma (Candidate) Multiple myeloma (Validated)	Swiss-Prot: P15941
<input type="checkbox"/> Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase	Protein	Cancer (Validated)	Swiss-Prot: P60484 PDB: 1D5R
<input type="checkbox"/> PLAU	Gene	Cancer (Validated) Cancer, breast (Validated) Cancer, head and neck (Validated) Cancer, ovary (Validated) Cancer, pancreas (Validated) Cancer, solid tumor (Validated) Female reproductive system cancer (Validated) Lesion, skin (Validated) Macular degeneration (Candidate) Ulcer, cutaneous chronic (Candidate)	GenBank: NM_002658 Entrez Gene: 5328
<input type="checkbox"/> PTEN	Gene	Cancer (Validated)	GenBank: NM_000314 Entrez Gene: 5728
<input type="checkbox"/> SERPINE1	Gene	Cancer (Candidate) Thrombosis (Validated) Thrombosis, arterial coronary (Candidate)	GenBank: M16006 Entrez Gene: 5054
<input type="checkbox"/> Steryl-sulfatase	Protein	Acne (Candidate)	Swiss-Prot: P08842

Display Formats

- ▶ Full Record List
- ▶ All Related Information
- ▶ Products
- ▶ References
- ▶ Patents
- ▶ Genomics

Refine in Chart Format

Therapeutic Target & Pathways
Charts available:

- ▶ Condition
- ▶ Mechanism of Action
- ▶ Type

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☐ Endothelial nitric
oxide synthase

☐ EPHA2

☐ Epidermal growth
factor receptor (isoform
a)

Gene

Protein

Angina pectoris (Validated)
Coronary artery disease (Candidate)
Heart failure, congestive (Validated)
Traumatic brain injury (Validated)

Cancer, solid tumor (Validated)

Astrocytoma (Validated)
Astrocytoma, anaplastic (Validated)
Cancer (Validated)
Cancer, biliary (Validated)
Cancer, bladder (Validated)
Cancer, brain (Candidate)
Cancer, breast metastatic (Validated)
Cancer, cervix (Validated)
Cancer, colon (Validated)
Cancer, colorectal (Validated)
Cancer, colorectal metastatic (Validated)
Cancer, esophagus (Validated)
Cancer, gastrointestinal (Validated)
Cancer, germ cells (Candidate)
Cancer, head and neck (Validated)
Cancer, kidney (Candidate)
Cancer, kidney (renal cell carcinoma) (Validated)
Cancer, kidney metastatic (Validated)
Cancer, larynx (Validated)
Cancer, liver (Validated)
Cancer, lung (non-small cell) (Validated)
Cancer, lung (non-small cell) metastatic (Validated)
Cancer, lung (small-cell) (Validated)
Cancer, mouth (Validated)
Cancer, ovary (Validated)
Cancer, pancreas (Validated)
Cancer, pancreas metastatic (Validated)
Cancer, prostate (Validated)
Cancer, rectum (Validated)
Cancer, rhinopharyngeal (Candidate)
Cancer, salivary glands (Validated)
Cancer, skin (Validated)
Cancer, solid tumor (Validated)
Cancer, stomach (Validated)
Cancer, thyroid (Validated)
Carcinoma, adrenocortical (Validated)
Carcinoma, squamous-cell (Validated)
Digestive/gastrointestinal cancer (Validated)
Glioblastoma (Validated)
Glioblastoma multiforme (Validated)
Glioma (Validated)

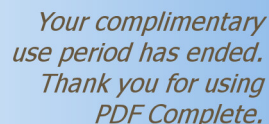
**See full record for
EGFR**

GenBank: NM_004431

Entrez Gene: 1969

Swiss-Prot: P00533

PDB: 1IVO, 1M14, 1M17, 1MOX, 1NQL



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PROUŠ S C I E N C E

Therapeutic Targets and Pathways

Full record for EGFR

Search

1 to 1 records retrieved from 1

Epidermal growth factor receptor (isoform a)		
Type	Protein	
Related Names	Avian erythroblastic leukemia viral (v-erb-b) oncogene homolog; EGFR variant 1; ERBB; ERBB1; Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian), transcript variant 1; HER1	
EC	2.7.10.1	
Links	Swiss-Prot: P00533 PDB: 1IVO , 1M14 , 1M17 , 1MOX , 1NQL	
Description/Function	<p>The epidermal growth factor receptor (EGFR; erbB1) is the prototype of a family of tyrosine kinases, called ErbB, that participate in the control of differentiation, proliferation and cell survival. ErbB family is comprised of erbB1 (HER-1/EGFR), erbB2 (HER-2), erbB3 (HER-3) and erbB4 (HER-4), all of which play important roles in development but that are often found dysregulated and/or overexpressed in premalignant and malignant breast tumors. EGFR is activated upon ligand binding to its extracellular domain, leading to dimerization and autophosphorylation of the cytoplasmic domains, which subsequently serve as docking sites for signal transducers that activate diverse signaling pathways, such as Ras-Raf-MAPK, PI3K-Akt, PLC-gamma1, Src, STAT and others. The ligands of ErbB receptors belong to the EGF family of peptide growth factors, including EGF, TGF-alpha, amphiregulin and neuregulin subfamily. EGFR gene amplification, activating mutations, overexpression of EGFR ligands and loss of negative regulatory mechanisms are some of the mechanisms responsible for aberrant EGFR signaling in cancer.</p>	
Targetscape	Breast Cancer Targetscape Lung Cancer Targetscape Melanoma Targetscape	Colorectal Cancer Targetscape Prostate Cancer Targetscape

Display Formats

- ▶ All Related Information
- ▶ Products
- ▶ References
- ▶ Patents
- ▶ Genomics

Refine in Chart Format

Therapeutic Target & Pathways

Charts available:

- ▶ Condition
- ▶ Mechanism of Action
- ▶ Type

Therapeutic Targets and Pathways

Full record for EGFR

Search

1 to 1 records retrieved from 1

Epidermal growth factor receptor (isoform a)	
Type	Protein
Related Names	Avian erythroblastic leukemia viral (v-erb-b) oncogene ERBB1; Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian), transcript variant 1; HER1
EC	2.7.10.1
Links	Swiss-Prot: P00533 PDB: 1IVO , 1M14 , 1M17 , 1MOX , 1NQL
Description/Function	The epidermal growth factor receptor (EGFR; erbB1) is the prototype of a family of tyrosine kinases, called ErbB, that participate in the control of differentiation, proliferation and cell survival. ErbB family is comprised of erbB1 (HER-1/EGFR), erbB2 (HER-2), erbB3 (HER-3) and erbB4 (HER-4), all of which play important roles in development but that are often found dysregulated and/or overexpressed in premalignant and malignant breast tumors. EGFR is activated upon ligand binding to its extracellular domain, leading to dimerization and autophosphorylation of the cytoplasmic domains, which subsequently serve as docking sites for signal transducers that activate diverse signaling pathways, such as Ras-Raf-MAPK, PI3K-Akt, PLC-gamma1, Src, STAT and others. The ligands of ErbB receptors belong to the EGF family of peptide growth factors, including EGF, TGF-alpha, amphiregulin and neuregulin subfamily. EGFR gene amplification, activating mutations, overexpression of EGFR ligands and loss of negative regulatory mechanisms are some of the mechanisms responsible for aberrant EGFR signaling in cancer.
Targetscape	<div>Breast Cancer Targetscape</div> <div>Colorectal Cancer Targetscape</div> <div>Lung Cancer Targetscape</div> <div>Prostate Cancer Targetscape</div> <div>Melanoma Targetscape</div>

Links to external databases with records on EGFR

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- ▶ All Related Information
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Refine in Chart Format

- Therapeutic Target & Pathways
Charts available:
- ▶ Condition
 - ▶ Mechanism of Action
 - ▶ Type

Links available from the
 full record include direct
 link to the Swiss-Prot
 entry for this target

1 to 1 re

Epidermal growth factor receptor (isoform a)	
Type	Protein
Related Names	Avian erythroblastic leukemia viral (v-erb-b) oncogene homolog; EGFR variant 1; ERBB; ERBB1; Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian), transcript variant 1; HER1
EC	2.7.10.1
Links	Swiss-Prot: P00533
Description/Function	The epidermal growth factor receptor (EGFR) is a member of the ErbB family of tyrosine kinases, called ErbB, that participate in cell growth and survival. ErbB family is comprised of ErbB1, ErbB2, ErbB3, and erbB4 (HER-4), all of which are overexpressed and/or overactivated upon ligand binding to the extracellular domain, leading to autophosphorylation of the cytoplasmic domain and activation of downstream signaling molecules such as Akt, PLC-gamma1, Src, STAT and others. EGFR gene amplification and loss of negative regulatory mechanisms lead to aberrant EGFR signaling in cancer.
Targetscape	Breast Cancer Targetscape Lung Cancer Targetscape Melanoma Targetscape

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All Related Information Products References

UniProtKB/Swiss-Prot entry P00533

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Entry history

[\[Entry info\]](#) [\[Name and origin\]](#) [\[References\]](#) [\[Comments\]](#) [\[Cross-references\]](#) [\[Keywords\]](#) [\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information	
Entry name	EGFR_HUMAN
Primary accession number	P00533
Secondary accession numbers	O00688 O00732 P06268 Q14225 Q92795 Q9BZS2 Q9GZX1 Q9H2C9 Q9H3C9 Q9UMD7 Q9UMD8 Q9UMG5
Integrated into Swiss-Prot on	July 21, 1986
Sequence was last modified on	November 1, 1997 (Sequence version 2)
Annotations were last modified on	December 4, 2007 (Entry version 124)
Name and origin of the protein	
Protein name	Epidermal growth factor receptor [Precursor]
Synonyms	EC 2.7.10.1 Receptor tyrosine-protein kinase ErbB-1
Gene name	Name: EGFR Synonyms: ERBB1
From	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorhini; Catarrhini; Hominidae; Homo.
Protein existence	1: Evidence at protein level;
References	
<p>[1] NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1). DOI=10.1038/309418a0; PubMed=6328312 [NCBI, Expasy, EBI, Israel, Japan] Ullrich A., Coussens L., Hayflick J.S., Dull T.J., Gray A., Tam A.W., Lee J., Yarden Y., Libermann T.A., Schlessinger J., Downward J., Mayes E.L.V., Whittle N., Waterfield M.D., Seeburg P.H.; "Human epidermal growth factor receptor cDNA sequence and aberrant expression of the amplified gene in A431 epidermoid carcinoma cells". Nature 309:418-425(1984).</p> <p>[2] NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 2).</p>	

Therapeutic Targets and Pathways

Links available from the
full record include direct
link to the Protein Data
Bank entry for this target

Type	Protein
Related Names	Avian erythroblastic leukemia viral (v-erb-b) oncogene homolog; EGFR variant 1; ERBB; ERBB1; Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian), transcript variant 1; HER1
EC	2.7.10.1
Links	Swiss-Prot: P00533 PDB: 1IVO, 1M14, 1M17, 1M18
Description/Function	The epidermal growth factor kinases, called ErbB, that pa survival. ErbB family is comp and erbB4 (HER-4), all of wh dysregulated and/or overexp activated upon ligand binding autophosphorylation of the c for signal transducers that a Akt, PLC-gamma1, Src, STA family of peptide growth fact subfamily. EGFR gene amplifi and loss of negative regulato aberrant EGFR signaling in c
Targetscape	Breast Cancer Targetscape Lung Cancer Targetscape Melanoma Targetscape

Display Formats

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1ivo DOI 10.2210/pdb/1ivo/pdb

Red - Derived Information

Title	Crystal Structure of the Complex of Human Epidermal Growth Factor and Receptor Extracellular Domains.
Authors	Ogiso, H., Ishitani, R., Nureki, O., Fukai, S., Yamanaka, M., Kim, J.H., Saito, K., Shirouzu, M., Yokoyama, S., RIKEN Structural Genomics/Proteomics Initiative (RSGI)
Primary Citation	Ogiso, H., Ishitani, R., Nureki, O., Fukai, S., Yamanaka, M., Kim, J.H., Saito, K., Inoue, M., Shirouzu, M., Yokoyama, S. (2002) Crystal Structure of the Complex of Human Epidermal Growth Factor and Receptor Extracellular Domains. <i>Cell</i> (Cambridge, Mass.) 110 : 775-787 [Abstract]
History	Deposition 2002-03-28 Release 2002-10-16
Experimental Method	Type X-RAY DIFFRACTION Data N/A
Parameters	Resolution[A] R-Value R-Free Space Group 3.30 0.258 (obs.) 0.326 P 3 ₁ 2 1
Unit Cell	Length [A] a 220.16 b 220.16 c 113.12 Angles [°] alpha 90.00 beta 90.00 gamma 120.00

Images and Visualization

Biological Molecule

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* Capable of displaying biological molecules.

Therapeutic Targets and Pathways

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Prous Science medical writers provide a short overview of each target's importance in pathological process

Epidermal growth factor receptor (isoform 1)	
Type	Protein
Related Names	Avian erythroblastic leukemia viral (v-erb-b) oncogene homolog; EGFR variant 1; ERBB; ERBB1; Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian), transcript variant 1; HER1
EC	2.7.10.1
Links	Swiss-Prot: P00533 PDB: 1IVO , 1M14 , 1M17 , 1MOX , 1NOL
Description/Function	The epidermal growth factor receptor (EGFR; erbB1) is the prototype of a family of tyrosine kinases, called ErbB, that participate in the control of differentiation, proliferation and cell survival. ErbB family is comprised of erbB1 (HER-1/EGFR), erbB2 (HER-2), erbB3 (HER-3) and erbB4 (HER-4), all of which play important roles in development but that are often found dysregulated and/or overexpressed in premalignant and malignant breast tumors. EGFR is activated upon ligand binding to its extracellular domain, leading to dimerization and autophosphorylation of the cytoplasmic domains, which subsequently serve as docking sites for signal transducers that activate diverse signaling pathways, such as Ras-Raf-MAPK, PI3K-Akt, PLC-gamma1, Src, STAT and others. The ligands of ErbB receptors belong to the EGF family of peptide growth factors, including EGF, TGF-alpha, amphiregulin and neuregulin subfamily. EGFR gene amplification, activating mutations, overexpression of EGFR ligands and loss of negative regulatory mechanisms are some of the mechanisms responsible for aberrant EGFR signaling in cancer.
Targetscape	<div>Breast Cancer Targetscape</div> <div>Colorectal Cancer Targetscape</div> <div>Lung Cancer Targetscape</div> <div>Prostate Cancer Targetscape</div> <div>Melanoma Targetscape</div>

Display Formats

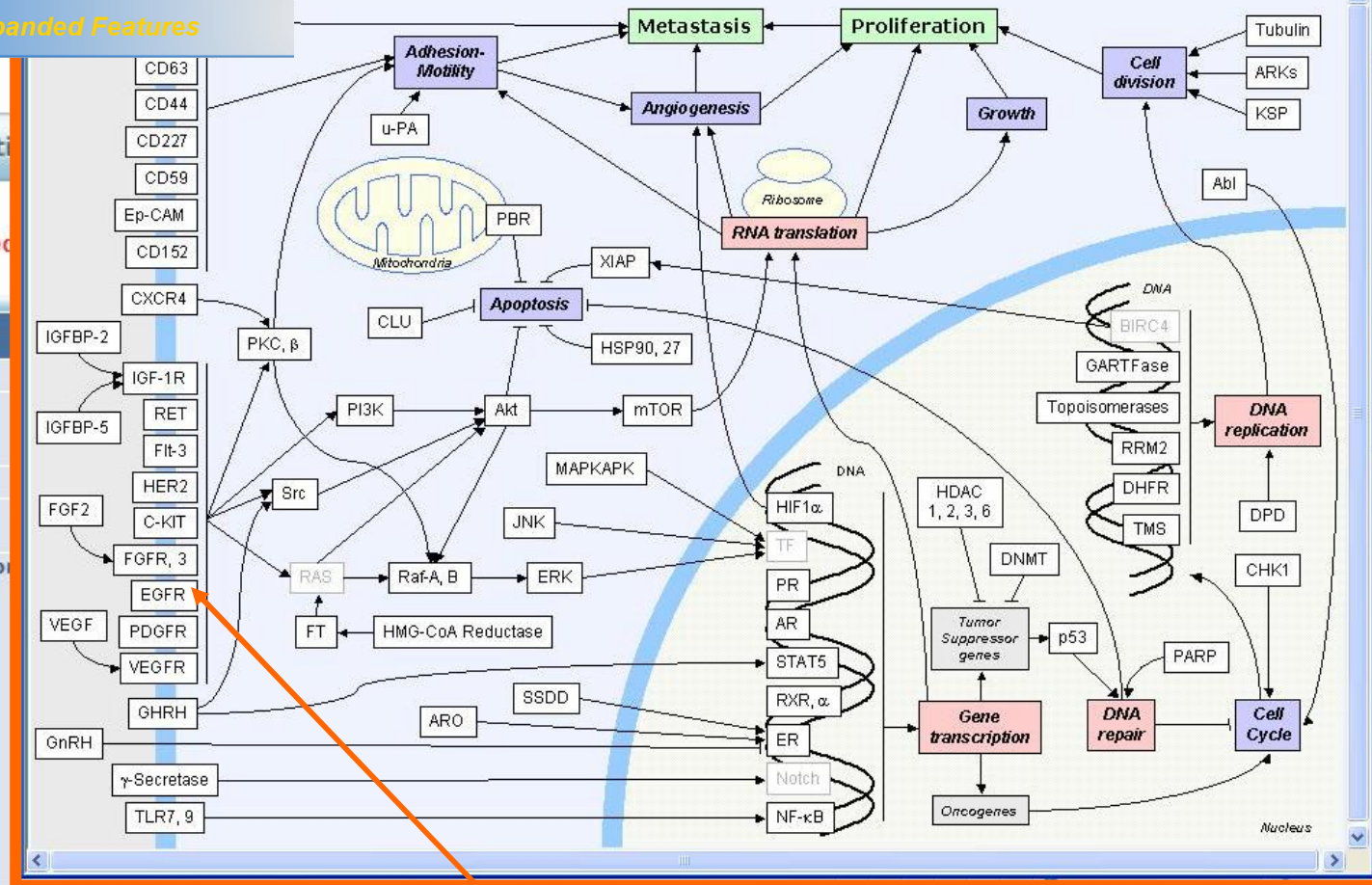
- ▶ All Related Information
- ▶ Products
- ▶ References
- ▶ Patents
- ▶ Genomics

Refine in Chart Format

Therapeutic Target & Pathways Charts available:

- ▶ Condition
- ▶ Mechanism of Action
- ▶ Type

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See the molecular landscapes
showing the involvement of
key targets in different
disease processes

Therapeutic Targets and Pathways

1 to 1 records retrieved from 1

Epidermal growth factor receptor (isoform a)					
Type	Protein				
Related Names	Avian erythroblastic leukemia viral (v-erb-b) oncogene homolog; EGFR variant 1; ERBB; ERBB1; Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian), transcript variant 1; HER1				
EC	2.7.10.1				
Links	Swiss-Prot: P00533 PDB: 1IVO , 1M14 , 1M17 , 1MOX , 1NQL				
Description/Function	The epidermal growth factor receptor (EGFR; erbB1) is the prototype of a family of tyrosine kinases, called ErbB, that participate in the control of differentiation, proliferation and cell survival. ErbB family is comprised of erbB1 (HER-1/EGFR), erbB2 (HER-2), erbB3 (HER-3) and erbB4 (HER-4), all of which play important roles in development but that are often found dysregulated and/or overexpressed in premalignant and malignant breast tumors. EGFR is activated upon ligand binding to its extracellular domain, leading to dimerization and autophosphorylation of the cytoplasmic domains, which subsequently serve as docking sites for signal transducers that activate diverse signaling pathways, such as Ras-Raf-MAPK, PI3K-Akt, PLC-gamma1, Src, STAT and others. The ligands of ErbB receptors belong to the EGF family of peptide growth factors, including EGF, TGF-alpha, amphiregulin and neuregulin subfamily. EGFR gene amplification, activating mutations, overexpression of EGFR ligands and loss of negative regulatory mechanisms are some of the mechanisms responsible for aberrant EGFR signaling in cancer.				
Targetscape	<table><tr><td>Breast Cancer Targetscape</td><td>Colorectal Cancer Targetscape</td></tr><tr><td>Lung Cancer Targetscape</td><td>Melanoma Targetscape</td></tr></table>	Breast Cancer Targetscape	Colorectal Cancer Targetscape	Lung Cancer Targetscape	Melanoma Targetscape
Breast Cancer Targetscape	Colorectal Cancer Targetscape				
Lung Cancer Targetscape	Melanoma Targetscape				

Display Formats

- ▶ All Related Information
- ▶ Products
- ▶ References
- ▶ Patents
- ▶ Genomics

Refine in Chart Format

Therapeutic Target & Pathways
Charts available:

- ▶ Condition
- ▶ Mechanism of Action
- ▶ Type

**Scroll down for further data
on this therapeutic target**

Carcinoma (Validated)	Astrocytoma, anaplastic (Validated)	Cancer (Validated)
Biliary (Validated)	Cancer, bladder (Validated)	Cancer, brain (Candidate)
Cancer, breast metastatic (Validated)	Cancer, cervix (Validated)	Cancer, colon (Validated)
Carcinoma, squamous-cell (Validated)	Digestive/gastrointestinal cancer (Validated)	Glioblastoma (Validated)
Glioblastoma multiforme (Validated)	Glioma (Validated)	Infection, coccidial (Validated)
Leukemia, acute myeloid (Validated)	Melanoma, metastatic (Validated)	Menetrier's disease (Validated)
Multiple myeloma (Validated)	Neuroblastoma (Validated)	Neurofibrosarcoma (Candidate)
	(Candidate)	Sarcoma (Candidate)

**Multimedia animations
illustrate in greater
detail pathological processes
and therapeutic pathways**

Images & Pathways

EGFR/HER2 Signal Transduction Pathways

Radioimmunotherapy: The Use of
Radiolabeled Antibodies in the Therapy of
Cancer

Resistance to Anti-HER2 Therapy



Related Mechanisms Products Under Development and Launched

EGFR (HER1; erbB1) Inhibitors; Anti-EGFR

▼ Cancer

▼ Infections

Related Information

Drugs & Biologics

626

Literature

26

Patents

12

Genomics

1

Biomarkers

1

Therapeutic Targets & Pathways

1

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		Carcinoma (Validated)	Astrocytoma, anaplastic (Validated)	Cancer (Validated)
		Biliary (Validated)	Cancer, bladder (Validated)	Cancer, brain (Candidate)
		Cancer, breast metastatic (Validated)	Cancer, cervix (Validated)	Cancer, colon (Validated)
		Carcinoma, squamous-cell (Validated)	Digestive/gastrointestinal cancer (Validated)	Glioblastoma (Validated)
		Glioblastoma multiforme (Validated)	Glioma (Validated)	Infection, coccidial (Validated)
		Leukemia, acute myeloid (Validated)	Melanoma, metastatic (Validated)	Menetrier's disease (Validated)
		Multiple myeloma (Validated)	Neuroblastoma (Validated)	Neurofibrosarcoma (Candidate)
Images & Pathways		Oligodendroglioma (Validated)	Psoriasis (Candidate)	Sarcoma (Candidate)
		Synovial sarcoma (Validated)		
		EGFR/HER2 Signal Transduction		
Related Mechanisms		Resistance to Anti-HER2 Therapy		
		EGFR (HER1; erbB1) Inhibitors; Anti-EGFR		
Products Under Development and Launched		▼ Cancer		
		▼ Infections		

See which other research groups are developing molecules using the same target

Related Information

Drugs & Biologics	626	Literature	26	Patents	12	Genomics	1
Biomarkers	1	Therapeutic Targets & Pathways	1				

**Start networking or
keeping an eye on the
competition!**

	Drug Name	Mechanism of Action	Organization	Phases
027	ior egf/r3	Inhibitors of Signal Transduction Pathways Anti-EGFR	Center of Molecular Immunology	Launched - 1995
230562	Cetuximab	Angiogenesis Inhibitors Inhibitors of Signal Transduction Pathways Anti-EGFR	Merck KGaA	Phase II
272554	Technetium nimotuzumab	Anti-EGFR	YM BioSciences	Phase I/II
304403	SAI-EGFR-ECD	Anti-EGFR	Center of Molecular Immunology YM BioSciences	Predclinical Predclinical
384901	HKI-357	Inhibitors of Signal Transduction Pathways EGFR (HER1; erbB1) Inhibitors	Wyeth Pharmaceuticals	Predclinical
396354	ARRY-334543	HER2 (erbB2) Inhibitors EGFR (HER1; erbB1) Inhibitors	Array BioPharma	Phase I
447851	CUDC-101	HER2 (erbB2) Inhibitors EGFR (HER1; erbB1) Inhibitors Histone Deacetylase (HDAC) Inhibitors	Curis	Predclinical

▲ Infections

▲ Infection, protozoal

▲ Infection, coccidial

EN	Drug Name	Mechanism of Action	Organization	Phases
383388	RM-6427	EGFR (HER1; erbB1) Inhibitors	Romark	Predclinical

Related Information

Drugs & Biologics	626	Literature	26	Patents	12	Genomics	1
Biomarkers	1	Therapeutic Targets & Pathways	1				

	Drug Name	Mechanism of Action	Organization	Phases
027	ior egf/r3	Inhibitors of Signal Transduction Pathways Anti-EGFR	Center of Molecular Immunology	Launched - 1995
230562	Cetuximab	Angiogenesis Inhibitors Inhibitors of Signal Transduction Pathways Anti-EGFR	Merck KGaA	Phase II
272554	Technetium nimotuzumab	Anti-EGFR	YM BioSciences	Phase I/II
304403	SAI-EGFR-ECD	Anti-EGFR	Center of Molecular Immunology YM BioSciences	Predclinical Predclinical
384901	HKI-357	Inhibitors of Signal Transduction Pathways EGFR (HER1; erbB1) Inhibitors	Wyeth Pharmaceuticals	Predclinical
396354	ARRY-334543	HER2 (erbB2) Inhibitors EGFR (HER1; erbB1) Inhibitors	Array BioPharma	Phase I
447851	CUDC-101	HER2 (erbB2) Inhibitors EGFR (HER1; erbB1) Inhibitors Histone Deacetylase (HDAC) Inhibitors	Curis	Pred

Search results are indexed and structured around 12 interlinked Knowledge Areas

▲ Infections

▲ Infection, protozoal

▲ Infection, coccidial

EN	Drug Name	Mechanism of Action	Organization	Phases
383388	RM-6427	EGFR (HER1; erbB1) Inhibitors	Romark	Predclinical

Related Information

Drugs & Biologics	626	Literature	26	Patents	12	Genomics	1
Biomarkers	1	Therapeutic Targets & Pathways	1				

Click here for a list of
molecules acting on
EGFR as a target

	Drug Name	Mechanism of Action	Organization	Phases
027	ior egf/r3	Inhibitors of Signal Transduction Pathways Anti-EGFR	Center of Molecular Immunology	Launched - 1995
230562	Cetuximab	Angiogenesis Inhibitors Inhibitors of Signal Transduction Pathways Anti-EGFR	Merck KGaA	Phase II
272554	Technetium nimotuzumab	Anti-EGFR	YM BioSciences	Phase I/II
304403	SAI-EGFR-ECD	Anti-EGFR	Center of Molecular Immunology YM BioSciences	Predclinical Predclinical
384901	HKI-357	Inhibitors of Signal Transduction Pathways EGFR (HER1; erbB1) Inhibitors	Wyeth Pharmaceuticals	Predclinical
4	ARRY-334543	HER2 (erbB2) Inhibitors EGFR (HER1; erbB1) Inhibitors	Array BioPharma	Phase I
447851	CUDC-101	HER2 (erbB2) Inhibitors EGFR (HER1; erbB1) Inhibitors Histone Deacetylase (HDAC) Inhibitors	Curis	Predclinical

▲ Infections

▲ Infection, protozoal

▲ Infection, coccidial

EN	Drug Name	Mechanism of Action	Organization	Phases
383388	RM-6427	EGFR (HER1; erbB1) Inhibitors	Romark	Predclinical

Related Information

Drugs & Biologics

626

Literature

26

Patents

12

Genomics

1

Biomarkers

1

Therapeutic Targets & Pathways

1

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Drugs & Biologics

Products related to Target "EGFR (erbB1)"

1 to 25 records retrieved from 626

**We have now jumped
to the Drugs &
Biologics Knowledge
Area for the results
related to EGFR as a
target**

1 2 3 4 5 6 7 8 9 10 Next> Last>>

	IPortal ID	Code Name	Generic Name	Brand Name	Indication	Mechanism of Action Group	Organization	Highest Phase
<input type="checkbox"/> *	122175 FULL RECORD	PTI-G4660 SIPI-9764-I	Genistein	Bonistein	Cancer, kidney metastatic Fibrosis, cystic Osteopenia Cancer, prostate Cancer, bladder Endometrial hyperplasia Melanoma, metastatic	Apoptosis Inducers; CFTR Channel Activators; Tyrosine Kinase Inhibitors; EGFR (HER1; erbB1) Inhibitors; Angiogenesis Inhibitors; DNA Topoisomerase II Inhibitors; Inhibitors of Signal Transduction Pathways	SurModics Astellas Pharma Universita degli Studi di Messina National Cancer Institute (US) Bausch & Lomb National Institutes of Health	Phase II
<input type="checkbox"/> *	131055 FULL RECORD	LNS-5662	Quercetin		Pain	EGFR (HER1; erbB1) Inhibitors; Protein Tyrosine Phosphatase PTP-1B Inhibitors; Aldose Reductase Inhibitors; Cytokine Production Inhibitors; Xanthine Oxidase Inhibitors;	University of Shizuoka Limerick NeuroSciences	Phase I

Display Formats

- Full Record List
- Structure Activity
- All Related Information
- References

Refine in Chart Format

Compounds by:

- Development Status
- Therapeutic Impact (by Therapeutic Group)
- Organizational Benchmark
- Patents by Mechanism Scope
 - Molecular Mechanisms
 - Cellular Mechanisms
- Product Launches by Year
- Products and Targets (by Target)
- Conditions
- Under Active Development
- Agency (FDA, EMEA, etc)

Drugs & Biologics

Search

Products related to Target "EGFR (erbB1)"

1 to 25 records retrieved from 626

1 2 3 4 5 6 7 8 9 10 Next> Last>>

	IPortal ID	Code Name	Generic Name	Brand Name	Indication	Mechanism of Action Group	Organization	Highest Phase
<input type="checkbox"/>	122175 FULL RECORD	PTI-G4660 SIPI-9764-I	Genistein	Bonistein	Cancer, kidney metastatic Fibrosis, cystic Osteopenia Cancer, prostate Cancer, bladder	Apoptosis Inducers; CFTR Channel Activators; Tyrosine Kinase Inhibitors; EGFR (HER1; erbB1) Inhibitors; Angiogenesis Inhibitors; DNA Topoisomerase II Inhibitors; Inhibitors of Signal Transduction Pathways	SurModics Astellas Pharma Universita degli Studi di Messina National Cancer Institute (US) Bausch & Lomb National Institutes of Health	Phase II
<input type="checkbox"/>	131055 FULL RECORD	LNS-5662	Quercetin		Pain	EGFR (HER1; erbB1) Inhibitors; Protein Tyrosine Phosphatase PTP-1B Inhibitors; Aldose Reductase Inhibitors; Cytokine Production Inhibitors; Xanthine Oxidase Inhibitors;	University of Shizuoka Limerick NeuroSciences	Phase I

Refine search by
regulatory agency

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- References

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Compounds by:

- Development Status
- Therapeutic Impact (by Therapeutic Group)
- Organizational Benchmark
- Patents by Mechanism Scope
 - Molecular Mechanisms
 - Cellular Mechanisms
- Product Launches by Year
- Products and Targets (by Target)
- Conditions
- Under Active Development
- Agency (FDA, EMEA, etc)

Agency (FDA, EMEA, etc)

Select only those
molecules approved by
the Food & Drug
Administration (FDA)...



Display Options

 Horizontal Display

 Vertical Display

 Pie Chart Display

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Agency (FDA, EMEA, etc)

...and view the subset
of results

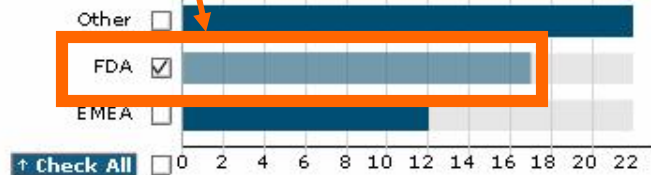
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 **View Subset(s)**

 Print Chart

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Drugs & Biologics

Search

1 to 17 records retrieved from 17

1

	IPortal ID ▲	Code Name	Generic Name	Brand Name	Indication	Mechanism of Action Group	Organization	Highest Phase ▼
<input type="checkbox"/>	301036 FULL RECORD	016 572016 GW-2016 GW-572016 GW-572016F	Lapatinib ditosylate	Tykerb Tyverb	Cancer, breast metastatic Cancer, head and neck Lymphoma, non- Hodgkin's Cancer, stomach Cancer, prostate Cancer, colorectal Cancer, gallbladder Cancer, hepatobiliary Glioblastoma multiforme Cancer, breast Cancer, peritoneum Cancer, solid tumor Esophageal carcinoma Cancer, intraductal Cancer, brain Cancer, ovary Cancer, pancreas metastatic Cancer, cervix	EGFR (HER1; erbB1) Inhibitors; HER2 (erbB2) Inhibitors; Inhibitors of Signal Transduction Pathways	GlaxoSmithKline Brown University National Cancer Institute (US)	Launched- 2007
<input type="checkbox"/>	276195 FULL RECORD	ABX-EGF E7.6.3	Panitumumab	Vectibix	Cancer, head and neck Carcinoma, squamous- cell Cancer, colorectal metastatic Cancer, lung (non-small cell)	Anti-EGFR; Inhibitors of Signal Transduction Pathways	Amgen	Launched- 2006
<input type="checkbox"/>	250837 FULL RECORD	CP-358774 NSC-718781 OSI-774 R-1415 Ro-50-8231	Erlotinib hydrochloride	Tarceva	Cancer, head and neck Cancer, breast metastatic Cancer, kidney (renal cell carcinoma)	EGFR (HER1; erbB1) Inhibitors; Inhibitors of Signal	University of California, Davis Schwarz Pharma	Launched- 2004

Display Formats

- Full Record List
- Structure Activity
- All Related Information
- References

Refine in Chart Format

Compounds by:

- Development Status
- Therapeutic Impact (by
Therapeutic Group)
- Organizational Benchmark
- Patents by Mechanism Scope
 - Molecular Mechanisms
 - Cellular Mechanisms
- Product Launches by Year
- Products and Targets (by
Target)
- Conditions
- Under Active Development
- Agency (FDA, EMEA, etc)

Drugs & Biologics

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View the full record
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1

	IPortal ID	Code Name	Generic Name	Brand Name	Indication	Mechanism of Action Group	Organization	Highest Phase
<input type="checkbox"/>	301036	016 572016 GW-2016 GW-572016 GW-572016F	Lapatinib ditosylate	Tykerb Tyverb	Cancer, breast metastatic Cancer, head and neck Lymphoma, non- Hodgkin's Cancer, stomach Cancer, prostate Cancer, colorectal Cancer, gallbladder Cancer, hepatobiliary Glioblastoma multiforme Cancer, breast Cancer, peritoneum Cancer, solid tumor Esophageal carcinoma Cancer, intraductal Cancer, brain Cancer, ovary Cancer, pancreas metastatic Cancer, cervix	EGFR (HER1; erbB1) Inhibitors; HER2 (erbB2) Inhibitors; Inhibitors of Signal Transduction Pathways	GlaxoSmithKline Brown University National Cancer Institute (US)	Launched- 2007
<input type="checkbox"/>	276195	ABX-EGF E7.6.3	Panitumumab	Vectibix	Cancer, head and neck Carcinoma, squamous- cell Cancer, colorectal metastatic Cancer, lung (non-small cell)	Anti-EGFR; Inhibitors of Signal Transduction Pathways	Amgen	Launched- 2006
<input type="checkbox"/>	250837	CP-358774 NSC-718781 OSI-774 R-1415 Ro-50-8231	Erlotinib hydrochloride	Tarceva	Cancer, head and neck Cancer, breast metastatic Cancer, kidney (renal cell carcinoma)	EGFR (HER1; erbB1) Inhibitors; Inhibitors of Signal	University of California, Davis Schwarz Pharma	Launched- 2004

Display Formats

- Full Record List
- Structure Activity
- All Related Information
- References

Refine in Chart Format

Compounds by:

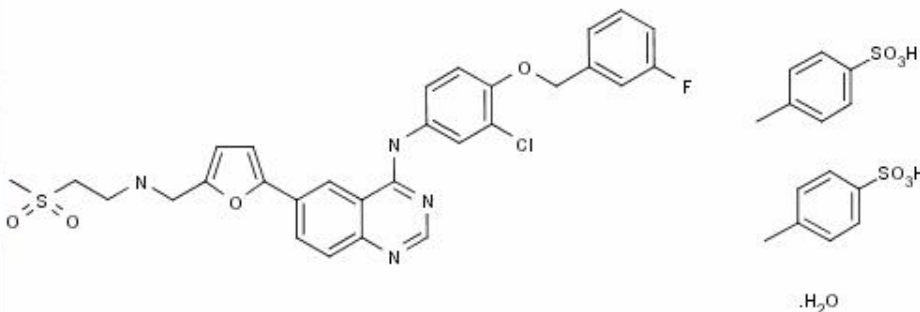
- Development Status
- Therapeutic Impact (by
Therapeutic Group)
- Organizational Benchmark
- Patents by Mechanism Scope
 - Molecular Mechanisms
 - Cellular Mechanisms
- Product Launches by Year
- Products and Targets (by
Target)
- Conditions
- Under Active Development
- Agency (FDA, EMEA, etc)

Full record for lapatinib

Drugs & Biologics

Search

1 to 1 records retrieved from 1

Lapatinib ditosylate		1 of 1
IPortal ID	301036	Structure 
CAS Registry No.	388082-78-8 231277-92-2 (free base, anhydrous) 388082-77-7 (anhydrous)	
Highest Phase	Launched-2007	
Molecular Formula	C43H44ClFN4O11S3	
Under Active Development		
Chemical Name / Description N-[3-Chloro-4-(3-fluorobenzyloxy)phenyl]-6-[5-[2-(methylsulfonyl)ethylaminomethyl]furan-2-yl]quinazolin-4-amine bis(4-methylbenzenesulfonate) hydrate		
Code Name	Generic Name	Brand Name
016 572016 GW-2016 GW-572016 GW-572016F	Lapatinib ditosylate	Tykerb Tyverb
Indication		Cellular / Molecular Mechanism
Cancer, breast metastatic Cancer, head and neck Lymphoma, non-Hodgkin's Cancer, stomach Cancer, prostate Cancer, colorectal Cancer, gallbladder Cancer, hepatobiliary Glioblastoma multiforme		EGFR (HER1; erbB1) Inhibitors HER2 (erbB2) Inhibitors Inhibitors of Signal Transduction Pathways

Product Description

phostins

Organization

GlaxoSmithKline
Brown University
National Cancer Institute (US)

Lapatinib, an ErbB-1 and ErbB-2 dual kinase inhibitor, was launched in the U.S. in 2007 for the treatment of advanced or metastatic HER2 (ErbB2) positive breast cancer in women who have received prior therapy, including Herceptin(R) (trastuzumab), in combination with Xeloda(R) (capecitabine). The compound was approved in 2007 in Switzerland and Australia for this indication and regulatory applications have been filed in Japan and Canada. Phase III trials are under way to evaluate the use of lapatinib as first-line treatment of breast cancer and head and neck cancer and for use in combination with paclitaxel in patients with ErbB2 amplified advanced gastric cancer. The compound is also being evaluated for several oncologic indications in the treatment of brain, gallbladder, prostate, ovary, endometrium, cervical and hepatobiliary cancers in collaboration with the National Cancer Institute (NCI). Lapatinib in combination with everolimus is also in early clinical studies for the treatment of lymphoma and non-Hodgkin's lymphoma (NHL). A phase I/II combination trial is evaluating lapatinib for the treatment of advanced or metastatic colorectal cancer. The National Cancer Institute (NCI) is developing the compound in phase II trials for the treatment of peritoneal cancer, ovarian and ductal carcinoma in situ of the breast (DCIS), while Brown University is conducting combination trials with gemcitabine for the treatment of pancreas metastatic cancer. Lapatinib was granted fast-track status by the FDA in 2005 for the treatment of refractory advanced or metastatic breast cancer patients who have documented ErbB-2 overexpression and who have failed previous therapy.

Development Status Summary

DETAILS

MILESTONES

REGULATORY INFORMATION

Phase	Organization	Indication
Launched - 2007	GlaxoSmithKline	Cancer, breast metastatic
Phase III	GlaxoSmithKline	Cancer, breast
Phase III	GlaxoSmithKline	Cancer, head and neck
Phase III	GlaxoSmithKline	Cancer, stomach
Phase II	National Cancer Institute (US)	Cancer, brain
Phase II	GlaxoSmithKline	
Phase II	National Cancer Institute (US)	
Phase II	National Cancer Institute (US)	
Phase II	National Cancer Institute (US)	
Phase II	National Cancer Institute (US)	
Phase II	Brown University	
Phase II	National Cancer Institute (US)	
Phase II	GlaxoSmithKline	Cancer, peritoneum
Phase II	GlaxoSmithKline	Cancer, prostate
Phase II	GlaxoSmithKline	Cancer, solid tumor
Phase II	GlaxoSmithKline	Esophageal carcinoma
Phase II	National Cancer Institute (US)	Glioblastoma multiforme
Phase I/II	GlaxoSmithKline	Cancer, colorectal
Phase I/II	National Cancer Institute (US)	Cancer, intraductal
Phase I	National Cancer Institute (US)	Cancer, breast
Phase I	National Cancer Institute (US)	Cancer, solid tumor
Phase I	National Cancer Institute (US)	Lymphoma, non-Hodgkin's

Search results are
indexed and structured
around 12 interlinked
Knowledge Area

Related Information

Literature	331	Intellectual Property	25	Experimental Pharmacology	141	Pharmacokinetics / Metabolism	149
Clinical Studies	137	Therapeutic Targets & Pathways	3	Adverse Events	209	Biomarkers	25

Product Description

phostins

Organization

GlaxoSmithKline
Brown University
National Cancer Institute (US)

Lapatinib, an ErbB-1 and ErbB-2 dual kinase inhibitor, was launched in the U.S. in 2007 for the treatment of advanced or metastatic HER2 (ErbB2) positive breast cancer in women who have received prior therapy, including Herceptin(R) (trastuzumab), in combination with Xeloda(R) (capecitabine). The compound was approved in 2007 in Switzerland and Australia for this indication and regulatory applications have been filed in Japan and Canada. Phase III trials are under way to evaluate the use of lapatinib as first-line treatment of breast cancer and head and neck cancer and for use in combination with paclitaxel in patients with ErbB2 amplified advanced gastric cancer. The compound is also being evaluated for several oncologic indications in the treatment of brain, gallbladder, prostate, ovary, endometrium, cervical and hepatobiliary cancers in collaboration with the National Cancer Institute (NCI). Lapatinib in combination with everolimus is also in early clinical studies for the treatment of lymphoma and non-Hodgkin's lymphoma (NHL). A phase I/II combination trial is evaluating lapatinib for the treatment of advanced or metastatic colorectal cancer. The National Cancer Institute (NCI) is developing the compound in phase II trials for the treatment of peritoneal cancer, ovarian and ductal carcinoma in situ of the breast (DCIS), while Brown University is conducting combination trials with gemcitabine for the treatment of pancreas metastatic cancer. Lapatinib was granted fast-track status by the FDA in 2005 for the treatment of refractory advanced or metastatic breast cancer patients who have documented ErbB-2 overexpression and who have failed previous therapy.

Development Status Summary

DETAILS

MILESTONES

REGULATORY INFORMATION

Phase	Organization	Indication
Launched - 2007	GlaxoSmithKline	Cancer, breast metastatic
Phase III	GlaxoSmithKline	Cancer, breast
Phase III	GlaxoSmithKline	Cancer, head and neck
Phase III	GlaxoSmithKline	Cancer, stomach
Phase II	National Cancer Institute (US)	Cancer, brain
Phase II	GlaxoSmithKline	Cancer, cervix
Phase II	National Cancer Institute (US)	Cancer, gallbladder
Phase II	National Cancer Institute (US)	Cancer, head and neck
Phase II	National Cancer Institute (US)	Cancer, hepatobiliary
Phase II	National Cancer Institute (US)	Cancer, ovary
Phase II	Brown University	pancreas metastatic
Phase II	National Cancer Institute (US)	peritoneum
Phase II	GlaxoSmithKline	state
Phase II	GlaxoSmithKline	solid tumor
Phase II	GlaxoSmithKline	carcinoma
Phase II	National Cancer Institute (US)	Glioblastoma multiforme
Phase I/II	GlaxoSmithKline	Cancer, colorectal
Phase I/II	National Cancer Institute (US)	Cancer, intraductal
Phase I	National Cancer Institute (US)	Cancer, breast
Phase I	National Cancer Institute (US)	Cancer, solid tumor
Phase I	National Cancer Institute (US)	Lymphoma, non-Hodgkin's

[Click here to see the
list of clinical studies
related to this molecule](#)

Related Information

Literature

331

Intellectual Property

25

Experimental Pharmacology

141

Pharmacokinetics / Metabolism

149

Clinical Studies

137

Therapeutic Targets & Pathways

3

Adverse Events

209

Biomarkers

25

**The list of clinical
studies related to this
molecule**

Clinical Studies

Clinical Studies related to Lapatinib ditosylate (EN 301036)

1 to 25 records retrieved from 57

1 2 3

Journal/Congresses (57)

Other Sources (80)

Study	Design	Pop.No.	Drug Name	Conclusions / Objectives	Ref.
<input type="checkbox"/> Lapatinib in prostate cancer	Multicenter Open	23	Lapatinib ditosylate	Lapatinib was well tolerated but ineffective in patients with prostate cancer	Ref. 1
<input type="checkbox"/> Chemotherapy in biliary cancer	Comparative Pooled/meta-analysis Randomized	2810	Paclitaxel Gemcitabine Irinotecan hydrochloride Lanreotide acetate Docetaxel Erlotinib hydrochloride Lapatinib ditosylate Exatecan	Gemcitabine in combination with platinum was associated with high response and tumor control rates in patients with gallbladder carcinoma or cholangiocarcinoma	Ref. 2
<input type="checkbox"/> Lapatinib in stomach cancer	Open	47	Lapatinib ditosylate	A phase II study suggested that lapatinib was well tolerated but induced only moderate antitumor activity in patients with gastric cancer	Ref. 3
<input type="checkbox"/> Lapatinib plus topotecan in cancer	Dose-finding Multicenter Open	24	Topotecan hydrochloride Lapatinib ditosylate	The combination of lapatinib and topotecan was well tolerated in a phase I study; the maximum tolerated doses in patients with advanced solid tumors were 1250 mg/day and 4 mg/m ² /week, respectively	Ref. 4
<input type="checkbox"/> Lapatinib, gemcitabine and oxaliplatin in pancreas cancer	Open	15	Gemcitabine Oxaliplatin Lapatinib	The combination of lapatinib and full-dose gemcitabine was feasible in patients with pancreaticobiliary	Ref. 5

Display Formats

- Full Record List
- All Related Information
- References

Refine in Chart Format

Clinical Charts available:

- Clinical Study Design
- Clinical Study Population
- Clinical Study Condition
- Clinical Study Products

Product Description

phostins

Organization

GlaxoSmithKline
Brown University
National Cancer Institute (US)

Lapatinib, an ErbB-1 and ErbB-2 dual kinase inhibitor, was launched in the U.S. in 2007 for the treatment of advanced or metastatic HER2 (ErbB2) positive breast cancer in women who have received prior therapy, including Herceptin(R) (trastuzumab), in combination with Xeloda(R) (capecitabine). The compound was approved in 2007 in Switzerland and Australia for this indication and regulatory applications have been filed in Japan and Canada. Phase III trials are under way to evaluate the use of lapatinib as first-line treatment of breast cancer and head and neck cancer and for use in combination with paclitaxel in patients with ErbB2 amplified advanced gastric cancer. The compound is also being evaluated for several oncologic indications in the treatment of brain, gallbladder, prostate, ovary, endometrium, cervical and hepatobiliary cancers in collaboration with the National Cancer Institute (NCI). Lapatinib in combination with everolimus is also in early clinical studies for the treatment of lymphoma and non-Hodgkin's lymphoma (NHL). A phase I/II combination trial is evaluating lapatinib for the treatment of advanced or metastatic colorectal cancer. The National Cancer Institute (NCI) is developing the compound in phase II trials for the treatment of peritoneal cancer, ovarian and ductal carcinoma in situ of the breast (DCIS), while Brown University is conducting combination trials with gemcitabine for the treatment of pancreas metastatic cancer. Lapatinib was granted fast-track status by the FDA in 2005 for the treatment of refractory advanced or metastatic breast cancer patients who have documented ErbB-2 overexpression and who have failed previous therapy.

Development Status Summary

DETAILS

MILESTONES

REGULATORY INFORMATION

Phase	Organization	Indication
Launched - 2007	GlaxoSmithKline	Cancer, breast metastatic
Phase III	GlaxoSmithKline	Cancer, breast
Phase III	GlaxoSmithKline	Cancer, head and neck
Phase III	GlaxoSmithKline	Cancer, stomach
Phase II	National Cancer Institute (US)	Cancer, brain
Phase II	GlaxoSmithKline	Cancer, cervix
Phase II	National Cancer Institute (US)	Cancer, gallbladder
Phase II	National Cancer Institute (US)	Cancer, head and neck
Phase II	National Cancer Institute (US)	Cancer, hepatobiliary
Phase II	National Cancer Institute (US)	Cancer, ovary
Phase II	Brown University	pancreas metastatic
Phase II	National Cancer Institute (US)	peritoneum
Phase II	GlaxoSmithKline	state
Phase II	GlaxoSmithKline	solid tumor
Phase II	GlaxoSmithKline	carcinoma
Phase II	National Cancer Institute (US)	Glioblastoma multiforme
Phase I/II	GlaxoSmithKline	Cancer, colorectal
Phase I/II	National Cancer Institute (US)	Cancer, intraductal
Phase I	National Cancer Institute (US)	Cancer, breast
Phase I	National Cancer Institute (US)	Cancer, solid tumor
Phase I	National Cancer Institute (US)	Lymphoma, non-Hodgkin's

[Click here to look at the
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this drug](#)

Related Information

Literature

331

Intellectual Property

25

Experimental Pharmacology

141

Pharmacokinetics / Metabolism

149

Clinical Studies

137

Therapeutic Targets & Pathways

3

Adverse Events

209

Biomarkers

25

**Details of adverse
events reported for this
drug in clinical studies**

Adverse Events

Search

1 to 25 values retrieved from 209

1 2 3 4 5 6 7 8 9

	Drug Name▲	Mechanism of Action	Event▲	Population	Condition	Ref▲
<input type="checkbox"/>	Calcium folinate <small>ALL AE</small> 0.2 g/m2 i.v. o.d. x 2/2wks Fluorouracil <small>ALL AE</small> 0.4 g/m2 i.v. o.d. x 2/2wks Fluorouracil <small>ALL AE</small> 0.32 g/m2 i.v. o.d. x 2/2wks Lapatinib ditosylate <small>ALL AE</small> 1.25 g p.o. o.d. Oxaliplatin <small>ALL AE</small> 68·10 ⁻³ g/m2 i.v. 1x/2 wks	DNA Alkylating Drugs Antimitotic Drugs; Pyrimidine Antagonists Antimitotic Drugs; Pyrimidine Antagonists EGFR (HER1; erbB1) Inhibitors; HER2 (erbB2) Inhibitors; Inhibitors of Signal Transduction Pathways	Diarrhea (grade 1)	Humans; Adult	Cancer	Ref. 1
<input type="checkbox"/>	Calcium folinate <small>ALL AE</small> 0.2 g/m2 i.v. o.d. x 2/2wks Fluorouracil <small>ALL AE</small> 0.4 g/m2 i.v. o.d. x 2/2wks Fluorouracil <small>ALL AE</small> 0.32 g/m2 i.v. o.d. x 2/2wks Lapatinib ditosylate <small>ALL AE</small> 1.25 g p.o. o.d. Oxaliplatin <small>ALL AE</small> 68·10 ⁻³ g/m2 i.v. 1x/2 wks	DNA Alkylating Drugs Antimitotic Drugs; Pyrimidine Antagonists Antimitotic Drugs; Pyrimidine Antagonists EGFR (HER1; erbB1) Inhibitors; HER2 (erbB2) Inhibitors; Inhibitors of Signal Transduction	Diarrhea (grade 2)	Humans; Adult	Cancer	Ref. 1

Display Formats

- ▶ Full Record List
- ▶ All Related Information
- ▶ References

Refine in Chart Format

adverse events charts

- ▶ Product
- ▶ Population
- ▶ Adverse event
- ▶ Report type
- ▶ Mechanism

Product Description

phostins

Organization

GlaxoSmithKline
Brown University
National Cancer Institute (US)

Lapatinib, an ErbB-1 and ErbB-2 dual kinase inhibitor, was launched in the U.S. in 2007 for the treatment of advanced or metastatic HER2 (ErbB2) positive breast cancer in women who have received prior therapy, including Herceptin(R) (trastuzumab), in combination with Xeloda(R) (capecitabine). The compound was approved in 2007 in Switzerland and Australia for this indication and regulatory applications have been filed in Japan and Canada. Phase III trials are under way to evaluate the use of lapatinib as first-line treatment of breast cancer and head and neck cancer and for use in combination with paclitaxel in patients with ErbB2 amplified advanced gastric cancer. The compound is also being evaluated for several oncologic indications in the treatment of brain, gallbladder, prostate, ovary, endometrium, cervical and hepatobiliary cancers in collaboration with the National Cancer Institute (NCI). Lapatinib in combination with everolimus is also in early clinical studies for the treatment of lymphoma and non-Hodgkin's lymphoma (NHL). A phase I/II combination trial is evaluating lapatinib for the treatment of advanced or metastatic colorectal cancer. The National Cancer Institute (NCI) is developing the compound in phase II trials for the treatment of peritoneal cancer, ovarian and ductal carcinoma in situ of the breast (DCIS), while Brown University is conducting combination trials with gemcitabine for the treatment of pancreas metastatic cancer. Lapatinib was granted fast-track status by the FDA in 2005 for the treatment of refractory advanced or metastatic breast cancer patients who have documented ErbB-2 overexpression and who have failed previous therapy.

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Phase II	GlaxoSmithKline	Cancer, cervix
Phase II	National Cancer Institute (US)	Cancer, gallbladder
Phase II	National Cancer Institute (US)	Cancer, head and neck
Phase II	National Cancer Institute (US)	Cancer, hepatobiliary
Phase II	National Cancer Institute (US)	Cancer, ovary
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Phase II	National Cancer Institute (US)	peritoneum
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Phase II	GlaxoSmithKline	carcinoma
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Phase I/II	National Cancer Institute (US)	Cancer, intraductal
Phase I	National Cancer Institute (US)	Cancer, breast
Phase I	National Cancer Institute (US)	Cancer, solid tumor
Phase I	National Cancer Institute (US)	Lymphoma, non-Hodgkin's

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with this molecule](#)

Related Information

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Therapeutic Targets & Pathways

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Adverse Events

209

Biomarkers

25

**We are now in the
recently launched
Biomarkers
Knowledge Area**

1 to 25 records retrieved from 26

Biomarker Name▲	Indication	Role	Technique (Substrate)	Validity
<input type="checkbox"/> Bcl-2	Cancer, prostate	Prognosis	IHC (Tissue Protein)	Potential
<input type="checkbox"/> beta-Catenin	Cancer, colorectal	Prognosis	IHC (Tissue Protein)	Potential
		Differential Diagnosis	PCR + DirectSeq (DNA)	Potential
		Prognosis	IHC (Tissue Protein)	Potential
		Differential Diagnosis	IHC (Tissue Protein)	Potential
<input type="checkbox"/> CEA	Cancer	Prognosis - Disease	IA (Serum)	Established
		Monitoring		
		Prognosis - Disease	EIA ()	Established
		Monitoring		
<input type="checkbox"/> Chromogranin A	Cancer, colorectal	Staging	IA (Serum)	Established
	Cancer, lung	Diagnosis	IA (Plasma)	Potential
		Prognosis	IHC (Tissue Protein)	Potential
	Neuroendocrine cancer	Prognosis	IA (Plasma)	Potential
		Prognosis	RT-PCR (mRNA)	Under Investigation
		Diagnosis	IA (Plasma)	Potential
		Monitoring Treatment Efficacy	IA (Plasma)	Potential
<input type="checkbox"/> DPD	Cancer, colorectal	Selection for Therapy	RT-PCR (mRNA)	Under Investigation
	Neutropenia	Selection for Therapy	RT-PCR (mRNA)	Potential
		Predicting Treatment Toxicity	PCR (DNA)	Potential
<input type="checkbox"/> FHIT	Cancer, lung	Prognosis	IHC (Tissue Protein)	Potential
		Prognosis	PCR/LOH (DNA)	Potential
		Prognosis	RT-PCR (mRNA)	Under Investigation
		Prognosis	Methylation PCR (DNA)	Potential
<input type="checkbox"/> Fibrin/FDP	Coronary artery disease	Risk Factor - Cardiovascular		Under Investigation
<input type="checkbox"/> HE4	Cancer, ovary	Diagnosis	IHC (Tissue Protein)	Potential
<input type="checkbox"/> HER2	Cancer, breast	Selection for Therapy	IHC (Tissue Protein)	Established
		Selection for Therapy	FISH (DNA)	Established

Display Formats

- ▶ Full Record List
- ▶ All Related Information

Refine in Chart Format

Biomarkers charts available by:

- ▶ Diseases
- ▶ Role
- ▶ Validity
- ▶ Type
- ▶ Biological Process
- ▶ Technique
- ▶ Substrate
- ▶ Status
- ▶ Organization

1 to 25 records retrieved from 26

1 2

Biomarker Name▲	Indication	Role	Technique (Substrate)	Validity
<input type="checkbox"/> Bcl-2	Cancer, prostate	Prognosis	IHC (Tissue Protein)	Potential
<input type="checkbox"/> beta-Catenin	Cancer, colorectal	Prognosis Differential Diagnosis	IHC (Tissue Protein) PCR + DirectSeq (DNA)	Potential Potential
<input type="checkbox"/> CEA	Cancer	Prognosis - Disease Monitoring	IHC (Tissue Protein)	Potential
<input type="checkbox"/> Chromogranin A	Cancer, colorectal Cancer, lung Neuroendocrine cancer	Prognosis - Disease Monitoring Staging Diagnosis Prognosis Prognosis Diagnosis Monitoring Treatment Efficacy	IA (Serum) EIA () IA (Serum) IA (Plasma) IHC (Tiss IA (Plasm RT-PCR (C IA (Plasm IA (Plasm	Established Established Established Potential
<input type="checkbox"/> DPD	Cancer, colorectal Neutropenia	Selection for Therapy Selection for Therapy Predicting Treatment Toxicity	RT-PCR (mRNA) RT-PCR (mRNA) PCR (DNA)	Under Investigation Potential Potential
<input type="checkbox"/> FHIT	Cancer, lung	Prognosis Prognosis Prognosis Prognosis	IHC (Tissue Protein) PCR/LOH (DNA) RT-PCR (mRNA) Methylation PCR (DNA)	Potential Potential Under Investigation Potential
<input type="checkbox"/> Fibrin/FDP	Coronary artery disease	Risk Factor - Cardiovascular		Under Investigation
<input type="checkbox"/> HE4	Cancer, ovary	Diagnosis	IHC (Tissue Protein)	Potential
<input type="checkbox"/> HER2	Cancer, breast	Selection for Therapy Selection for Therapy	IHC (Tissue Protein) FISH (DNA)	Established Established

**Click to access the full
record for a given
biomarker**

Display Formats

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Refine in Chart Format

Biomarkers charts available by:

- ▶ Diseases
- ▶ Role
- ▶ Validity
- ▶ Type
- ▶ Biological Process
- ▶ Technique
- ▶ Substrate
- ▶ Status
- ▶ Organization

Full record for HER2 as a biomarker

Biomarkers

1 to 1 records retrieved from 1

HER2	
Synonym	EGFR2; ERBB2 ; Epidermal growth factor receptor 2; ErbB-2; HER2/Neu; NEU; Receptor protein-tyrosine kinase erbB-2; v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 2
Type	Proteomic; Genomic
Biological Process	Angiogenesis; Oncogenesis; Invasion; Tumor Cell Proliferation
Description	The human epidermal growth factor receptor 2 (HER2) is a transmembrane protein with an intracellular tyrosine kinase activity and an extracellular receptor domain. Most of the studies have linked either HER2 gene amplification or Her2 protein overexpression with adverse prognosis in either node-negative or node-positive disease. Another use of this marker in clinical practice is focused on the prediction of response to the anti-HER2 targeted therapy with trastuzumab, and with the small molecule anti-HER1/HER2 tyrosine kinase inhibitor lapatinib. HER2 assessment is most often used as a biomarker for therapy selection. Although HER2 testing is a standard of breast cancer management, it may also be useful to evaluate or manage prostate, colorectal or ovarian cancer.
Organization	Abbott Applied Biosystems Bayer Dako Genomic Health Invitrogen Oncor Roche Diagnostics Ventana Medical Vysis
Modifier	Product Modifier: Trastuzumab (Treatment) Lapatinib ditosylate (Treatment) Mechanism Modifier: HER2 (erbB2) Inhibitors (Treatment) Anti-HER2/neu/ErbB2 (Treatment)
Indications	Diseases

▲ Cancer, breast

Population	Role	Validity	Technique (Substrate)	Authority
	Selection for Therapy	Potential	SISH (DNA)	
	Selection for Therapy	Established	IHC (Tissue Protein)	FDA European Group on Tumour Markers (EGTM) ASCO
	Monitoring Treatment Efficacy	Potential	CISH (DNA)	
Metastatic	Prognosis - Disease Monitoring	Established	EIA (Tissue Protein)	FDA
Metastatic	Selection for Therapy	Potential	IHC (Tissue Protein)	
Metastatic	Selection for Therapy	Potential	RT-PCR (DNA)	
Metastatic	Selection for Therapy	Potential	eTAG (Protein)	
Stage II - Lymph Node Positive	Selection for Therapy	Established	FISH (DNA)	FDA European Group on Tumour Markers (EGTM) ASCO
Stage II - Lymph Node Positive	Selection for Therapy	Potential	RT-PCR (mRNA)	
Stage II - Lymph Node Positive	Monitoring Treatment Efficacy	Established	FISH (DNA)	FDA ASCO
Stage II - Lymph Node Positive	Prognosis	Established	FISH (DNA)	FDA European Group on Tumour Markers (EGTM) ASCO
Primary - Lymph Node Negative	Prognosis - Risk Stratification	Established	FISH (DNA)	FDA ASCO

▲ Digestive/gastrointestinal cancer

▲ Cancer, colorectal

Population	Role	Validity	Technique (Substrate)	Authority
Primary	Selection for Therapy	Potential	FISH (DNA)	



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The Translational Research Knowledge base

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