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Piramal Life Sciences

knowledge action care

ANNUAL REPORT

2007-2008

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The Board of Directors

Ajay G. Piramal, Chairman

Dr. (Mrs.) Swati A. Piramal, Vice-Chairperson

Gautam Doshi

Prof. Goverdhan Mehta

Dr. R. A. Mashelkar

Sir Ravinder Maini

N. Santhanam

Dr. Somesh Sharma, Managing Director

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Auditors

Price Waterhouse & Co., Mumbai.

Bankers

Axis Bank Limited

Calyon Bank

HDFC Bank Limited

ICICI Bank Limited

Kotak Mahindra Bank

Registered Office

Piramal Tower,
Ganpatrao Kadam Marg,
Lower Parel,
Mumbai 400 013, India.

The Gyana Mudra, which embodies Knowledge, Action and Care, has been adopted as the new logo by the Piramal Group. The front page carries a creative rendition of the Gyana Mudra by renowned artist Mr. Ravi Mandlik.

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The Vision

To discover, develop and commercialize innovative drugs to address still unmet medical needs to reduce the burden of disease.

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contents

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Chairman's Letter

Dear Shareholders,

Warm greetings to you all!

I am pleased to address you in the first annual report of Piramal Life Sciences Limited since listing of the company.

Pursuant to the composite scheme of Arrangement sanctioned by the Hon'ble Bombay High Court, the New Chemical Entity (NCE) Research unit of Piramal Healthcare Limited was demerged to the Company w.e.f. 1st April 2007. Our vision is to discover, develop and commercialize innovative drugs to address still unmet medical needs to reduce the burden of disease.

The Piramal Group, has derived insight and strength from Indian culture and philosophy. Our path is guided by our core values: Gyana Yoga (knowledge and learning), Karma Yoga (dynamic action and entrepreneurial spirit) and Bhakti Yoga (care and compassion), which are embodied in our new visual identity, our logo – the Gyan Mudra. We are confident that our new corporate identity and our values Knowledge, Action and Care, will spur us to democratize healthcare and empower the community and in return create value for our shareholders going forward.

The pharmaceutical industry globally is at a very exciting juncture with biotechnology and genetic engineering opening up new avenues. Pharmaceutical leaders are not significantly increasing the number of New Chemical Entities (NCEs) in their pipelines preferring instead to requisition Research and Development (R&D) boutiques that work at creating new molecular designs. On the other hand, the volume and complexity of work in the international markets that is required to bring an NCE to approval is increasing steadily. PLSL seeks to leverage on the tremendous scientific knowledge pool of India with the end objective of being able to provide affordable medicines to millions of patients across the globe.

Financial year 2007-08 marked steady performance for our Company. Two additional candidates: NPB-001-05 -a Phytopharmaceutical in Oncology and P-1201-07 -the candidate from our first collaboration with Eli Lilly in Metabolic Disorders have moved into clinical trials. Today, we have a pipeline of 15 drug candidates with 5 of them in clinical trials. Our lead molecule P-276 in Oncology continues to progress well and is currently undergoing Phase I/II studies in India, Canada and USA.

During the year we signed two new collaboration agreements with global pharmaceutical leaders. We signed an agreement with Merck and Co., Inc. to discover and develop new drugs for two targets in Oncology segment provided by Merck. We signed a second drug development agreement with Eli Lilly & Company, USA. The new alliance generally follows the framework established by the earlier agreement between PLSL and Eli Lilly and continues the rationale of seeking to increase productivity in drug development by synergising the unique strengths of both companies and equitably sharing risk and reward.

NCE Research is a long gestation activity. It takes 8-10 years from lead identification to commercial launch of a drug. It is a unique business model. With a pipeline of 15 candidates including 5 in clinical trials, our NCE Research unit has come a long way since its acquisition of the India R&D center from Hoechst in 1998. Our Company's accomplishments are a result of the dedication and commitment of its employees, partners, customers and shareholders.

I thank you for the belief and confidence that you have reposed in our innovative R&D business. With your support and encouragement, I am confident that our Company will achieve great success in the coming years.

Warm regards,

Ajay G. Piramal
Chairman

Date :31st May, 2008

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Management Discussion & Analysis

Review of the year ended 31 March 2008:

BUSINESS STRATEGY :

PLSL's drug discovery and development program is based on the following criteria:

- Significant unmet medical need
- Availability of scientifically validated therapeutic targets in well-understood biological pathways
- Relatively fast, well-defined path to clinical development
- Leverage strong in-house capabilities in:
  - Medicinal chemistry
  - Natural products chemistry
  - Biology
  - Animal pharmacology
- Leverage strong capability in early-phase development

Therapy areas & Pathway selection:

PLSL seeks to address pathways indicated in multiple applications. The Company's discovery and development is focused on the following four therapeutic areas:

- Oncology
- Inflammation
- Infectious Diseases
- Diabetes

PLSL therapeutic areas and biological targets

No	Therapy area	Biological targets
1	Oncology	• Cyclin Dependent Kinase Inhibitors • Hypoxia Inducible Factor-1a (HIF-1a) Inhibitors • PI3 Kinase Inhibitors
2	Inflammation	• TNF-∝ Production / Release Inhibitors • Safer NSAIDs
3	Diabetes & Metabolic disorders	• Insulin Sensitizers (non- PPARγ) • GPR40 Modulators
4	Infectious disease	• Microbial extracts: Antibacterials • Microbial extracts: Antifungals

Target selection:

PLSL's discovery strategy is to be an "early follower" by working on precedented and unprecedented targets that have been validated by leaders with late-stage, potentially first-in-class development candidates.

The Company does not work on classes of drugs where there are above five competitor candidates at a similar level of development.

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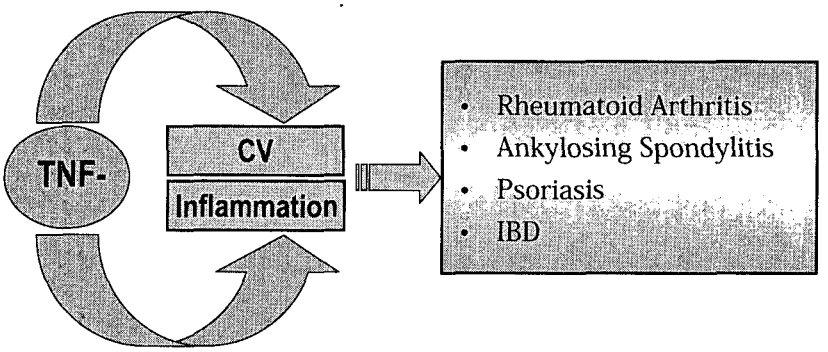
Pathway selection :

PLSL seeks to address pathways indicated in multiple applications:

Multiple application of TNF-∝ as a Target



Lead Identification:

PLSL's seeks to leverage India's bio-diversity and vast pool of knowledge in traditional medicinal systems such as Ayurveda and Siddha to source for drug lead molecules.

The Company has a unique and diverse collection of natural product extracts from microbes and plants from rare habitats in India, collected over a period of last three decades. It is probably the only drug Company in India with a collection of this kind in terms of size and diversity:

No.	Natural Product Extracts	Nos.
1	Plant extracts	5,600
2	Microbial strains	35,000

Discovery efforts include evaluation and investigation of medicinal extracts/ preparations from herbs and plants as cited in ancient Ayurvedic texts. PLSL seeks to bring phytopharmaceuticals to the world, by applying modern science and clinical validation techniques.

This approach has proved to be significantly less expensive and more rewarding compared to current, more common strategy of relying only on massive screening of vast combinatorial libraries of "druggable" compounds.

Development & Commercialisation Strategy:

PLSL plans to be a vertically integrated drug development Company, with the capability to take drug candidates from early discovery through clinical development and launch worldwide.

Being based in India, PLSL has the advantage of a large "treatment naïve" patient pool, lower clinical trial & overhead expenses, as well as availability of skilled scientists. The Company can discover and develop drugs at a fraction of what it costs big pharma Companies.

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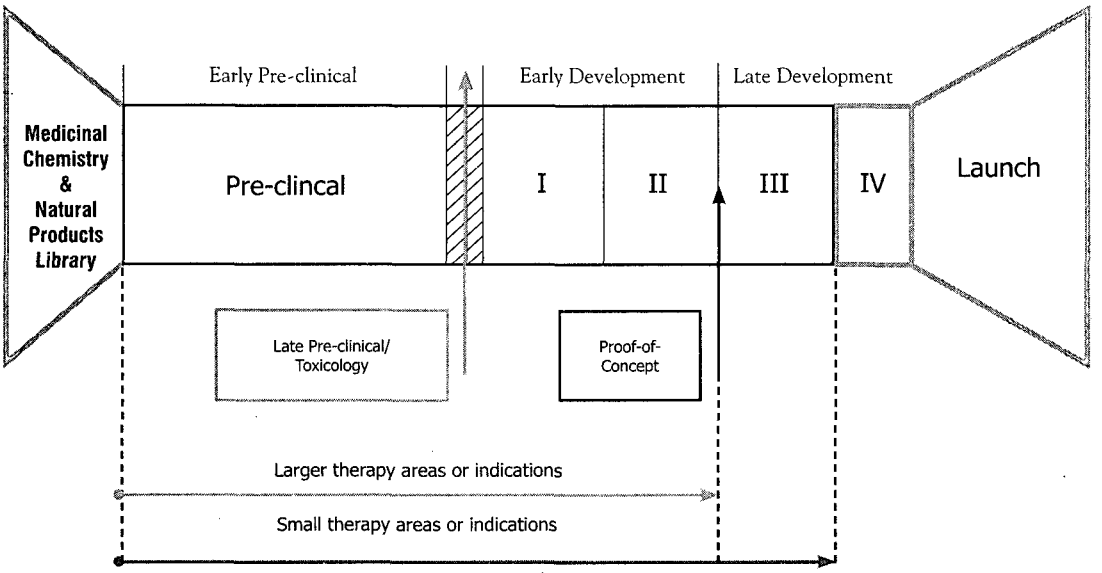
PLSL Discovery & Development Strategy



PLSL will take new chemical entities (NCEs) or plant extracts from early discovery through Phase II clinical trials in India and Overseas.

After Phase II, PLSL will pursue one of the following two pathways:

- Develop to Proof-of-Concept: Then, Out-license

  Discovery → Early Development (I & II) → Out-license

  Whenever the program or product involves larger clinical trials, PLSL will out-license to global pharmaceutical companies, after establishment of Proof-of-Concept (end of Phase II). In late-stage development, the two Companies will co-develop on a shared risk and reward basis. PLSL will concurrently continue Phase III trials in India.

- Carry-to-Market:

  Discovery → Early Development (I & II) →* Late Development (III) → Launch

  Whenever the program or product involves orphan drug status, niche indications, or accelerated clinical trials, PLSL will develop the compound through to launch.

In-licensing strategy: Pipeline expansion

As an innovator pharmaceutical Company, PLSL is committed to widening its pipeline, both with own as well as in-licensed drug candidates. In-licensing helps enhance the probability of success, by increasing "shots at the goal" for the Company.

PLSL does not pay an upfront fee in the in-licensing agreements. The Company bears pre-clinical and early stage (I and II) development costs, while the partner is responsible for late stage development (Phase III and IV), registration, and launch in developed markets.

PLSL has strong domain expertise in pre-clinical and early development. Its development speed is faster, while its costs are a fraction of western costs.

In a typical in-licensing agreement, PLSL would have the following rewards:

- Milestone payments based on successful result of Phase I and/or Phase II and/or Phase III (post-registration)
- A percentage royalty of global sales upon launch
- Exclusive marketing rights for India and/or additional South Asian markets

PLSL has in-licensing relationships with the following partners, based on the described risk-reward sharing mechanism:

1. Eli Lilly & Co.
2. Merck & Co.
3. Pierre Fabre Laboratories

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R&D Agreement with Eli Lilly & Co.:

In January 2007, PLSL signed a drug development agreement with Eli Lilly & Co. to develop and commercialize a select group of Lilly's pre-clinical drug candidates spanning multiple therapeutic areas.

As the first part of this agreement, Eli Lilly has given PLSL a patented pre-clinical compound, which is at an optimized lead stage:

- PLSL is responsible for design and execution of the global clinical development program up to end of Phase II, including IND-enabling non-clinical studies and human clinical trials
- Eli Lilly will be responsible for Phase III, registration, and launch worldwide (excluding India and certain South Asian countries).

PLSL will receive the following:

- Milestone payments on successful completion of Phase I, II and III, aggregating US$ 100 million
- Percentage royalty on global sales upon successful launch
- Exclusive marketing rights for India and certain neighboring countries

R&D Agreement with Merck & Co.:

In November 2007, Merck & PLSL entered into a research and development collaboration agreement to discover and develop new drugs for two new oncology targets provided by Merck.

PLSL will be responsible for carrying out an integrated drug discovery program from hits to leads through pre-clinical candidate selection, followed by investigational new drug (IND)-enabling non-clinical studies and human clinical trials demonstrating proof-of-concept, primarily for Oncology.

Merck will have an option to advance the most promising drug candidates into late stage clinical trials and to commercialize these drug candidates.

PLSL will receive the following:

- Milestone payments associated with progress in the development of drug candidate of up to US$ 175 million per target
- Royalties on global sales upon successful launch of the product
- Marketing rights for India and certain neighboring countries upon successful launch

R&D Agreement with Pierre Fabre Laboratories:

In January 2008, PLSL entered into a collaboration agreement with Pierre Fabre Laboratories for research in oncology.

The Pierre Fabre Group will provide expertise in screening and research in oncology, while PLSL will make available its natural products base, which will lead to the pharmacological characterisation of new molecules.

Collaborations with Academic Research Organisations:

PLSL has agreements with three Western and seven Indian academic research institutes for collaboration in discovery and development work:

1. National Research Council, Canada
2. Oncotest, Germany
3. De Montfort University, UK
4. Central Drug Research Institute, Lucknow, India
5. Indian Institute of Science, Bangalore, India
6. National Institute of Immunology, Delhi, India
7. Indian Institute of Chemical Biology, Kolkata, India
8. Anna University, Chennai, India
9. National Institute of Oceanography, Goa, India
10. Indian Institute of Chemical Biology, Kolkata, India

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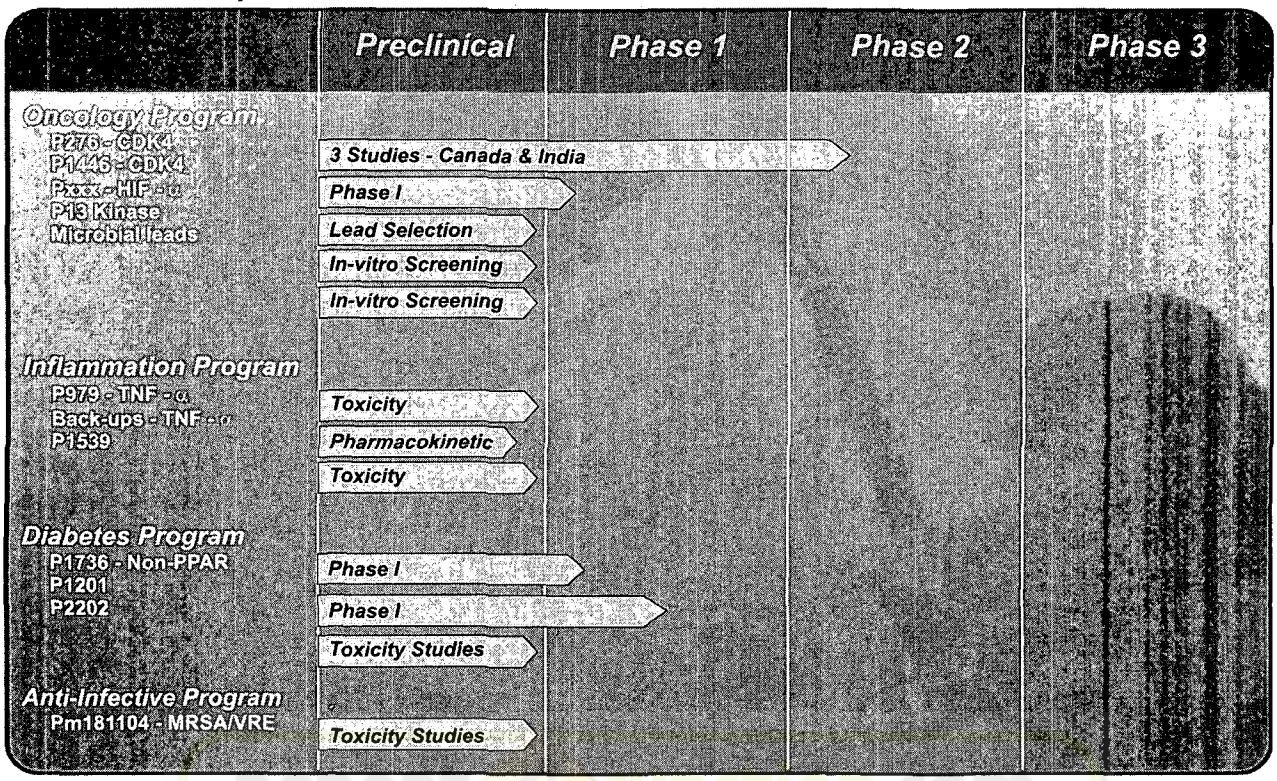
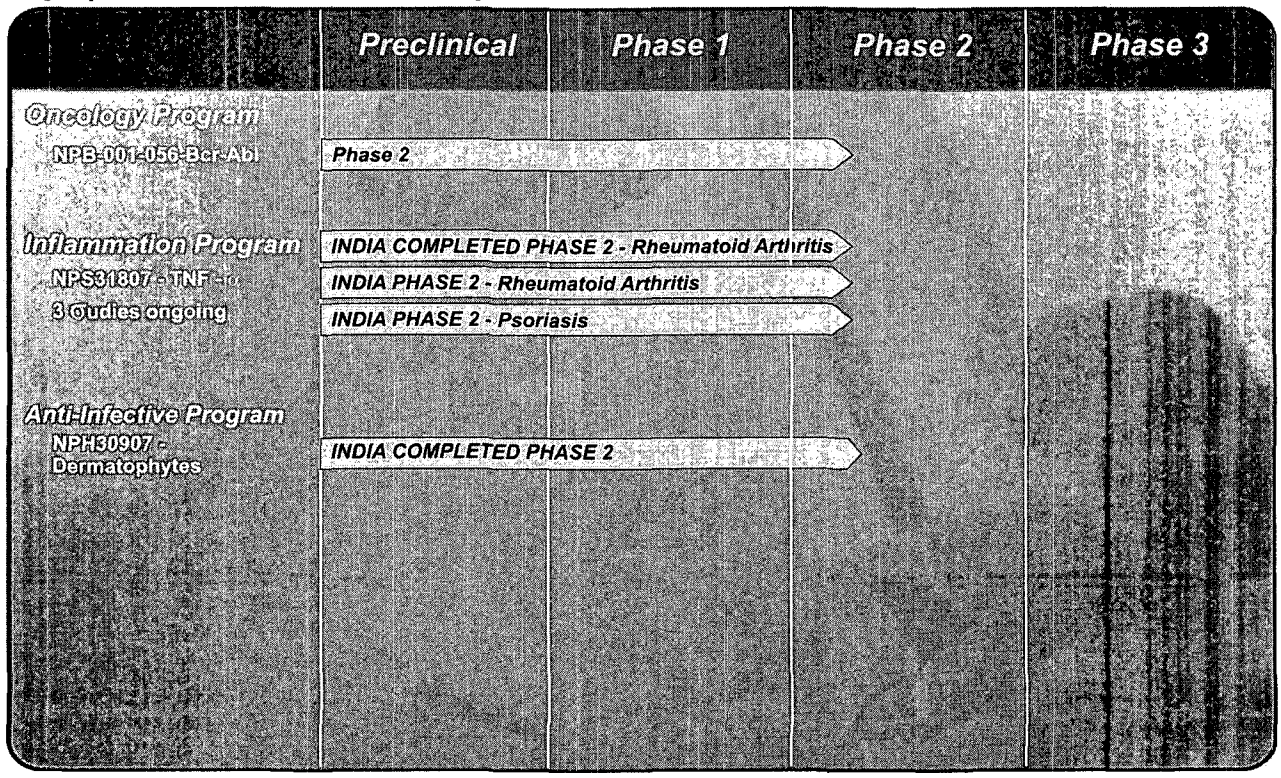
NCE - Current Pipeline Overview



Phytopharmaceutical - Current Pipeline Overview



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Clinical Stage Programs

ONCOLOGY

Cdk inhibitor program

Disease Background

Cancer continues to be a killer disease throughout the world and is the second leading cause of death after cardiovascular disease. All multiplying cells have to go through a process called as 'cell cycle'. The Cyclin dependent kinase (Cdk) complexes play an important role in regulation of cell cycle progression. Dysregulation of the cell cycle is considered to be one of the important mechanisms of cancer development. In human cancers, genetic and epigenetic events result in over expression of Cyclins or absent or diminished levels of Cdk inhibitors, which provide tumor cells a selective growth advantage. Inhibiting the Cyclins/Cdks therefore offers a potential mechanism for treatment of cancer.

P276

P276 is a novel potent small molecule flavone derived selective Cdk 4-D1, Cdk1-B and Cdk9-T inhibitor, with potent cytotoxic effects against tumor cell lines. Anti-tumor activity of P276-00 has also been demonstrated in cellular assays and in rodent tumor models. Phase I study of P276 conducted in India and Canada has been completed and has indicated a safe recommended phase II dose as 185 mg/m2/day administered from day 1 to day 5 in each 21 days cycle. The study has also shown initial efficacy signals in the form of stable disease for a duration ranging from 2 to 8 cycles in 13 subjects and reduction in tumor size in 2 subjects. We have also initiated, a phase I/II study in multiple myeloma (cancer of a specific type of white blood cells) across five centres in India in addition to a phase I study in multiple myeloma to be conducted across three centers in USA, which has been granted Investigational New Drug (IND) approval by US-FDA and the study is expected to be initiated soon. Having determined the recommended phase II dose from the completed phase I study, a proposal for phase II study in squamous cell carcinoma of head and neck (most common cancer in men in India) has been submitted to Drugs Controller General India DCG(I) and is awaiting the approval. We will soon embark on a global phase II studies in mantle cell lymphoma and malignant melanoma. In addition, since most of the cancers require multiple therapeutic modalities for their effective management, we also have plans for initiating studies of P276 in combination with gemcitabine (which is already approved for the treatment of pancreatic cancer) and in combination with radiation.

P1446

P1446 is a novel, selective, potent and orally active inhibitor of Cdk4 D1, Cdk1 B and Cdk9 T. This molecule would serve as a back-up molecule for P276. Studies with a variety of cancer cell lines suggest that P1446 effectively inhibits proliferation of and induces cytotoxicity in both cisplatin sensitive and resistant cells without any significant cytotoxicity to normal human cells. Oral administration of P1446 resulted in significant inhibition of tumor growth in rodent tumor models. Studies conducted in-house indicate a need of prolonged oral administration of P1446 for sustained effect. Proposal for phase I study of P1446 to be conducted in India has already been submitted to DCG(I) and the approval is expected soon. Additional phase I study to explore a continuous dosing schedule is also being planned to be initiated in North America.

Chronic myeloid leukemia

NPB001

Disease Background

Chronic myeloid leukemia or CML, a disease of blood cells, is clinically characterized by an excessive multiplication of variety of cells in the peripheral blood accompanied by overgrowth of the cells even in the bone marrow. The hallmark of CML is the Philadelphia (Ph) chromosome, which is the result of a reciprocal translocation between chromosomes 9 and 22. It encodes for a new, abnormal gene called BCR-ABL that produces BCR-ABL tyrosine kinase, an abnormal protein that leads to the overproduction of immature, poorly functioning white blood cells in CML. CML accounts for almost 15% of all leukemias with 4000-5000 new cases being diagnosed in the US alone every year.

Allogeneic stem cell transplantation is the most effective cure for CML till date. However, its widespread application in patients of CML is thwarted due to the limited availability of matching donors and its suitability only to patients less than 65 years of age, who can withstand the toxic effects of transplantation. The current medical therapy of CML includes tyrosine kinase inhibitors such as imatinib mesylate, dasatinib, nilotinib, interferon-α and cytoreductive agents such as hydroxyurea, busulfan, cytarabine and their combinations. Although effective and durable, the emergence of resistance and intolerability to tyrosine kinase inhibitors is the biggest drawback of continued therapy with them.

NPB001 is a phytopharmaceutical administered as an oral suspension. It has demonstrated tyrosine kinase inhibitor properties. Preclinically it has demonstrated cell death and inhibition of cell proliferation in BCR-ABL +ve imatinib sensitive as well as resistant cell lines with specific inhibition of the BCR-ABL tyrosine kinase. It has also shown efficacy in the rodent models by decreasing the size of implanted tumour.

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