

NATIONAL INSTITUTES OF HEALTH NATIONAL CANCER INSTITUTE Frederick Cancer Research and Development Center

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### To the Friends and Colleagues of Bob Pettit

It is a pleasure and privilege for me to extend my sincere congratulations to my good friend and colleague, Bob Pettit, on the occasion of his being honored by the International Foundation for Anticancer Drug Discovery. It was Bob who launched me on the quest for new drugs of natural origin for the treatment of cancer during the sabbatical year spent with him in 1972, and who further strengthened my commitment to this cause while working with him and his dedicated research group at the ASU Cancer Research Institute from 1979 through 1984.

Those of us who have shared in Bob's infectious enthusiasm for the exploration of Nature's chemical bounty for exciting new drugs know that his enthusiasm in this respect is closely matched by his love for the wonder and beauty of Nature. I treasure the memories of sharing many exhilarating hikes and "Symposia in the Wilderness" exploring the majesty of the canyons and mountains of the Southwest!

There were instances when these two major preoccupations had to compete for his valuable time. I remember the occasion in December, 1980, when Bob and several of his fellow CRI Nature-devotees, including our friends, the Elsworths from Cape Town, planned a hike in the Canyon to Phantom Ranch. Most of the party set out in good time to allow for the trip to the Grand Canyon and the hike to the bottom, and I offered to wait for Bob to complete some of his Institute tasks, having been assured that we would leave no later than noon. Needless to say, his devotion to chemistry and cancer treatment consumed the hours, and we eventually left Tempe at 4pm to arrive at the South Rim in snow flurries at about 7pm! Never one to be daunted by apparently adverse conditions, Bob launched off down the Kaibab trail in the dark, and I dutifully followed in his footsteps, illuminated by the weak glow of my small flashlight! We arrived at Phantom Ranch to find our colleagues somewhat alarmed (but not surprised!) by our late arrival. They had commandeered the "best" campsites, so Bob and I settled for second-best. Later that night, a storm caused a minor flood which rushed through our colleagues' tents, but left Bob and myself high and dry - further evidence of the "Pettit-Magic"!

Bob, I offer my very best wishes to you and your team for continued success in your fight to alleviate human suffering through discovering the wonders of Nature!

Gordon M. Cragg

Chief, Natural Products Branch

National Cancer Institute



National Institutes of Health National Cancer Institute Bethesda, Maryland 20892

October 15, 1998

To the Friends and Colleagues of Dr. G. Robert Pettit!

It is with great pleasure that I send my enthusiastic greetings on this wonderful occasion honoring one of the giants of American chemistry.

Bob and I have had a spectacular collaboration going back at least a dozen years, for no other group has been as productive as his in discovering new drugs that attack the important target that is the focus of my group's research. We work on microtubules, whose main component is the protein tubulin. Microtubules are the primary elements of the mitotic spindle. Thus, drugs that interact with tubulin, either by inhibiting the assembly or the disassembly of microtubules, interfere with cell division, and such drugs are important in the treatment of cancer, parasitic diseases, and, to a lesser extent, inflammatory diseases. Microtubules also support the shape of and permit mobility in nondividing cells. Thus, disturbing microtubules in cells can also interfere with angiogenesis (blood vessel formation) and metastasis (cancer spread to distant sites).

The first group of antitubulin drugs on which we worked together are the combretastatins. These are structurally simple molecules isolated from the South African tree *Combretum caffrum*. The most potent of these compounds was called combretastatin A-4, and Bob and his group, as well as many other chemists around the world, quickly synthesized both combretastatin A-4 and a large number of purely synthetic analogs in ample amounts for biochemical and pharmacological studies, for studies in animals, and for clinical trials. One of these analogs, a soluble form called "combretastatin A-4 prodrug," seems particularly effective as an inhibitor of tumor blood vessel growth.

The second group of compounds from Bob's lab that caught our attention were highly modified peptides originally isolated from the sea hare *Dolabella auricularia*. Two of these peptides, dolastatin 10 and dolastatin 15, are particularly important, and both again attack cells through an interaction with tubulin. Bob's group synthesized these important molecules from scratch, as well as numerous active analogs, providing ample supplies for all types of studies, including the initial clinical trials. As with the combretastatins, Bob's ground breaking work with the dolastatins caused many other chemists to undertake projects involving the synthesis of the naturally occurring dolastatins and related synthetic analogs.

The third group of antitubulin compounds that Bob and his group isolated were halichondrin B and a variety of structural analogs from marine sponges of the genera Axinella and Halichondria. These are very complex macrocyclic polyethers. While Japanese workers first described compounds of this class in print, Bob's work was independent and essential for the NCI's studies of halichondrin B. The antitubulin mechanism of action of halichondrin B was first suggested by a computer analysis devised by my NCI colleague Dr. Kenneth Paull

(a former postdoctoral fellow of Bob's). Dr. Paull developed a method of evaluating differential cytotoxicity data generated in the NCI cell screen and called the resulting computer algorithm "COMPARE." The activity of halichondrin B against tumor cells was a key finding in the validation of COMPARE analysis for predicting molecular mechanism from data obtained with cells. Besides this important result with halichondrin B, its unique properties as an antitubulin agent and its activity against animal tumors led to its selection as a drug development candidate. The material supplied by Bob, as well as his demonstration that one could actually obtain enough material from sponges, was essential for halichondrin B to progress so far towards clinical trials.

The fourth group of antitubulin compounds from Bob's lab came from a marine sponge of the *Spongia* genus, and Bob named them the spongistatins. These compounds are also macrocyclic polyethers, but they differ considerably in structure from the halichondrins. They are among the most cytotoxic compounds yet discovered, but thus far only very small amounts have been isolated. Nevertheless, they interact with tubulin in interesting ways, and they should become important drugs when either practical syntheses are developed or a richer natural source comes to light.

As important as our collaboration with Bob has been in the discovery and mechanistic description of new and useful antitubulin agents, I am awed by the realization that this only represents a small portion of his current and overall contributions to chemistry, cancer research, and drug development.

So hats off and three cheers for Bob on this wonderful occasion in his honor! And hats off and three cheers every day for his past, ongoing, and future scientific work!

With warm congratulations and best wishes.

Ernest Hamel, M.D., Ph.D.

Senior Investigator

Laboratory of Drug Discovery Research and Development

Developmental Therapeutics Program

Division of Cancer Treatment and Diagnosis

National Cancer Institute



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September 16, 1998

To the Friends and Colleagues of Dr. G. Robert Pettit:

I first met Dr. G. Robert Pettit ten years ago. I had just been appointed Executive Director of the Arizona Disease Control Research Commission. He spent hours with me in his small overcrowded office, explaining in non-technical language the process of discovery at the Cancer Research Institute. He related tales of diving under the ice cap in his wet suit in freezing temperatures in search of unique species of plants and animals. He related stories about being shadowed on his expeditions by Japanese and Soviet vessels. He described in detail how specimens are harvested daily by divers in exotic places around the globe and shipped in metal containers to Arizona State University for drying and processing. He showed me how active compounds are isolated and synthesized in the laboratory. Then, five hours later and already past 6 PM, he walked me to my car on the other side of the campus. As I left the parking garage, he stood in the middle of the street waving his arms to stop traffic so I could enter the street with maximum safety.

Over the past decade, we have kept in touch. I even worked for him for a while. My respect and admiration for Bob Pettit, as a scientist and human being, has deepened with time. To my mind, he has the "right stuff" to be awarded a Nobel Prize for his single-minded, life-long dedication to finding cures for cancer. He remains focused on this objective today and shows no signs of slowing down. The eventual production of anticancer drugs can take a decade or more from the time an active compound is discovered. For a researcher to find even one cure in a lifetime is reason enough to celebrate. If someone discovers six, ten, or twelve cures, they surely deserve a Nobel Prize. And Dr. Pettit stands today at the cusp of such a momentous accomplishment. If the Cancer Research Institute is the jewel in the crown of the nation's anticancer drug discovery program, Dr. Pettit is the brilliance behind the jewel. He is a model scientist.

Even though Dr. Pettit is the object of worldwide acclaim, he continues to possess a humble and gracious charm. His human qualities and gentle nature have had an immeasurable impact on my life, and I have tried to emulate him in my own work, but mostly in vain. I am proud and honored to know Bob Pettit and to call him my friend.

Sincerely,

Robert S. Byars, Ph.D.

Assistant Director, Operations





Cox Building, Room 640 100 Blossom Street Boston, Massachusetts 02114-2617 E-mail: chabner.bruce@mgh.harvard.edu Tel: 617 724-3200. Fax: 617 724-3166 Bruce A. Chabner, M.D.

Professor of Medicine
Chief, Hematology-Oncology
Clinical Director, MGH Cancer Center

October 2, 1998

To the friends and colleagues of Dr. G. Robert Pettit:

I am delighted to share with you my thoughts on Dr. G. Robert Pettit. Dr. Pettit is a unique scientist and person, widely admired for his many contributions to natural product research and his devotion to the cause of biodiversity in the service of mankind.

As Director of the Division of Cancer Treatment at the National Cancer Institute, I had many opportunities to consult with Dr. Pettit and to accept his wise advice. More than any other individual, he was responsible for the preservation of the natural product drug discovery program at the NCI, a program that supported both intramural and extramural research and that led to the discovery of some of the most important new drugs for cancer treatment. Dr. Pettit's own laboratory has identified the most interesting and promising natural products now under clinical investigation, many of which have unique biochemical properties and targets.

While Dr. Pettit's scientific accomplishments are well-known, his personal dynamism is appreciated by his close friends and family. If there ever was a person I would want in my foxhole during a battle, it would be Bob. He is a relentless runner, a courageous sailor in dangerous waters, a fearless adventurer in the presence of pirates and sharks (both the swimming kinds and those in a three piece suit), and a man driven by his conviction that you only have one opportunity to do good works. He never fails to shock me with his stories of his travels and his projects. He is, to be sure, a treasure of a scientist and person.

I wish you all a fine evening and my congratulations for your support and celebration of Bob Pettit's career in research.

Sincerely yours,

Bruce Chabner, M.D.

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October 12, 1998

George Robert Pettit, M.D. Director and Dalton Professor Cancer Research Institute Arizona State University

To the Friends and Colleagues of Dr. G. Robert Pettit:

It is with great admiration that all of us at the *Institute for Drug Development* at the Cancer Therapy & Research Center and The University of Texas Health Science Center at San Antonio wish to honor Dr. G. Robert Pettit at this special tribute event. Dr. Pettit has been a remarkably productive cancer researcher, isolating and synthesizing natural products for clinical trials.

Dr. Pettit has brought us such important compounds as bryostatin 1, combretastatin A-4, dolastatin 10, and dolastatin 15, as well as other important compounds.

We in San Antonio have had the privilege to work with Dr. Pettit on looking at the in vitro activity of these compounds against human colony-forming units. Indeed, we are now planning clinical trials for combretastatin A-4, which clearly has antiangiogenic activity.

There is absolutely no question whatsoever that Dr. Pettit is the most knowledgeable individual in the area of natural products and the preclinical development of new anticancer agents. He has my total admiration, as well as that of my colleagues.

Congratulations, Dr. Pettit, on this well-deserved occasion!

With best regards.

Sincerely.

Daniel D. Von Hoff, M.D., F.A.C.P.

Director, Institute for Drug Development

Cancer Therapy & Research Center

and

Clinical Professor of Medicine

Division of Medical Oncology

The University of Texas Health Science

Center at San Antonio

DVH:smc

<sup>•</sup> An Affiliate of the Cancer Therapy & Research Center • San Antonio, Texas •

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#### To the Friends and Colleagues of Bob Pettit

The sociological lesson that Bob Pettit gives to us is that we should direct our lives toward a purposeful scientific goal. The depth of our dedication is not always apparent to others at the beginning, and the method of reaching the goal may not even be self-evident. In Bob's case, it all started with hard work that gained focus and utilized every opportunity.

His first publications following the Ph.D. at Wayne State University dealt with steric requirements and methods of synthesis. Then, in 1960-1961, he burst into the journals with sophisticated papers on steroids and potential cancerocidal agents. The University of Maine had been a quiet place, when, suddenly, Bob's sound research work and inspired student direction were combining to reveal, partially, the intended long-term goal. The goal was further identified in a long series of papers on antineoplastic agents that continued at Arizona State University along with further contributions on steroids from amphibian sources. It became a pleasant habit to follow and applaud Bob's work.

The next phase was not yet as apparent as his investigation of the anticancer constituents from terrestrial plants and from amphibians, but the ground was laid in 1970 for following the promise of useful anticancer drugs based on sources from the sea, especially marine animals. From 1977 on, there was a burst of Pettit publications dealing with cytotoxic and antineoplastic living organisms of the deep. The logistics necessary for success rivaled those necessary for a climb up Mount Everest. Bob Pettit was totally responsible for the enterprise that included the following: a knowledge of marine biology; ocean transport; diving; collection, biological identification, and preservation of samples; extraction and separation; spectrographic evaluation and structural analysis; biological testing, general and specific; pharmacological testing and comparative evaluation; increasing amounts of the lead compounds available; exploration of aquaculture for production; preclinical development; and, finally, the three phases of clinical trials.

Has Bob's monumental effort been successful? Yes, indeed! For example, bryostatin 1 is very important as an antileukemia candidate. Spongistatins 1, 3, and 4 are remarkable for their source. Dolastatin is peptide-like and prevents assembly of tubulin. Dolastatin 10 is active against prostate cancer. Cephalostatins 1 and 7 are very active but, for clinical trial, required total synthesis (Fuchs @ Purdue) in order to have sufficient material. Auristatin PE, on clinical trial in Japan, has Arizona State ownership.

It is certainly appropriate to pay tribute to Bob Pettit, a modest, compassionate, versatile man and a total scientist with a most praiseworthy goal.

Melson J. Leonard Nelson J. Leonard

### **Christie CRC Research Centre**

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## To the friends and colleagues of Bob Pettit

Dear Bob

It is difficult to believe that you have been involved in drug discovery for over 40 years. Every time we meet I am impressed and stimulated by your boundless energy and infectious enthusiasm and it has made you an inspiration for many scientists, including myself.

Your contribution to natural product chemistry is legendary. This together with your desire to provide new anti-cancer agents, has resulted in a host of novel molecules. The isolation, structural elucidation, and clinical development of bryostatin 1 is an example of scientific excellence which spans several disciplines. This work could not have taken place without your skill, vision and determination to succeed.

On a personal level, I would like to thank you for the support you have given to me over the years. Our discussions have always left me wanting to go straight into the laboratory!

You are an inspiration, and a friend.

With fondest wishes.

Dr Alan T McGown

Section Head

Section of Drug Development and Imaging





National Institutes of Health National Cancer Institute Bethesda, Maryland 20892

October 21, 1998

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To the friends and colleagues of Dr. George Robert Pettit:

I write this letter to extend the special acknowledgment and congratulations on the part of the Developmental Therapeutics Program of the Division of Cancer Treatment and Diagnosis, National Cancer Institute, to Dr. Bob Pettit on the occasion of his having passed 40 years in service to cancer research. Dr. Pettit himself, as well as the corpus of work that is the expression of his life's effort, are of enormous encouragement to us at the National Cancer Institute. He has been a staunch supporter for the Institute's efforts to develop novel therapeutic agents for patients afflicted with cancer, and his own work has led to the discovery and entry into clinical trial of substances such as bryostatin and dolastatin 10. These agents are at the vanguard of our efforts to define new treatment approaches and hope for people with this dread disease.

Among the many attributes possessed by Bob Pettit is the boundless energy and enthusiasm which he brings to bear in pursuit of these goals. His enthusiasm is infectious, and his determination extraordinary. I myself, as well as the entire staff of NCI's Developmental Therapeutics Program, derive inspiration from Dr. Pettit. He is an important ally and indeed a "General" in the war against cancer. I extend my congratulations to him and wish Bob and his colleagues at the Arizona State University Cancer Research Institute all the best in the years to come.

Sincerely yours,

Edward A. Sausville, M.D., Ph.D., F.A.C.P.

Edward a. Sausuelle

Associate Director

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# To Bob Pettit: Honoree International Foundation for Anticancer Drug Discovery November 18<sup>th</sup>,1998

Only a few times in one's life do you meet individuals who have a profound impact on not only your life but on the lives of all those with whom that person comes in contact. Bob Pettit is such an individual.

Edie and I first met Bob years ago through the good auspices of Don and Sharon Ulrich while I was trustee of the Dalton Foundation. Then, as he continues to do now, Bob impressed us with the need of the Arizona State University Cancer Institute to continue its incredible work with cancer curative drugs. His mild mannered approach belies the incredible intensity and dedication that he brings to cancer research. His personal sacrifices have been huge, giving up many opportunities in the corporate world to give guidance to what is now becoming known as one of the most prolific cancer research institutes in the United States.

Bob Dalton and I came to know Bob Pettit very well during the earlier years of the ASU Cancer Institute. Dr Pettit's dedication and persistence impressed Bob Dalton so much that he provided ASU with its very first endowed chair, the *Dalton Chair of Medicinal Chemistry*.

Bob Pettit's hands-on approach to research takes him to the most remote parts of the earth where he still actively dives for the specimens needed to continue the work of the Institute. Never have we met in individual who has been so intensely and personally involved in the process of finding cancer drugs.

"The noblest question in the world "observed Benjamin Franklin, in *Poor Richard* "is what good may I do in it?" Whether by leading or prodding others, or contributing in the thick of all things to some larger cause, perseverance is crucial to success. But, like most other virtues, persistence and perseverance cannot operate for good in the world in isolation from other virtues. Bob brings the right combination of intelligence, perseverance, dedication, and a high degree of moral integrity that is particularly needed in today's society.

Bob Bennett recently wrote a best seller called the *Book of Virtues* and in this book he quotes an anonymous author as follows:

When things go wrong, as they sometimes will, When the road you're charging seems all uphill, When the funds are low and the debts are high And you want to smile, but you have to sigh, When care is pressing you down a bit, Rest! If you must — but never quit.

Bob, thank you for all you continue to do.

John and Edie Reyno



Department of Chemistry and Biochemistry Main Campus PO Box 871604 Tempe, AZ 85287-1604 LeRoy Eyring Regents Professor Emeritus Phone: (602) 965-7088 FAX: (602) 965-2747 E-Mail: LEyring@asu.edu

Scottsdale, Arizona October 20, 1998

To the Friends and Colleagues of Dr. Bob Pettit:

I have been Bob's friend and colleague since he arrived at Arizona State University in 1965. This was just four years after the PhD degree was authorized for bestowal by the University and we were hiring the faculty that would bolster our teaching and research capacity to validate that highest of academic degrees in chemistry. Bob came with that promise. This Tribute Dinner suggests the level at which this promise was fulfilled. Not only was his mastery of the principles of chemistry superb but also his skill in their application to research. Above all, his dedication to the pursuit of new knowledge has been an inspiration to his many students and colleagues.

Bob is a brilliant synthesizer of the most complicated organic chemical compounds. I have known many brilliant scientists over a lifetime as an academic chemist. Such individuals possess intellectual prowess coupled with disciplined application of their peculiar understanding of scientific principles and their creative application.

Bob pursues his scientific interests with singleness of purpose. This is a hallmark of the greatest professors I have known. They see deep significance to their topic of inquiry and are committed to widening its understanding and acceptance. Nothing can be allowed to stand in the way of achievement of their goals. If obstacles cannot be surmounted they must be circumnavigated.

Bob is a humanitarian with concern for his fellow men. He is aware of the most poignant needs of their condition. His instinct is to be of service by finding a solution to their most difficult problems. These are admirable traits not always found among his gifted brethren.

Bob is a natural organizer, a born CEO. He can visualize what is required to accomplish a goal He can put these requirements into the hands of capable colleagues for their achievement. Furthermore, he is able and willing to step into the trenches beside his coworkers to guide and assist them in their accomplishments. He is also aware that success in chemical research of this type requires a great deal of material support.

It is rare almost to the point of being unique that all these qualities should reside in one individual. It is this combination of gifts that brings us here tonight to pay tribute to Bob's signal accomplishments.

Perhaps a few other bits of information about Bob are needed to help round out the picture. For example, it would not be unusual for Bob to lead a group of hikers from the north rim of the Grand Canyon down to the river by some trail that you had never heard of. He might just organize an annual tennis tournament to help fund his research. When Bob tells you, "When I get up each morning, the chemistry of natural products is so exciting that I hardly know which way to run first!" you wonder if he is for real. Many years of observation have convinced me that he is, indeed, the genuine article. In conversation he confides in such a way that you think the two of you are the only right-thinking pair on the planet.

I appreciate the warmth of Bob's fleeting attention interspersed rarely among the swiftly flowing episodes of his, chock full of adventure, life. This frantic search to discover cures for the most dreaded disease of his fellowman has taken him to the edges of human knowledge and to strange creations at the ends of the earth.

LeRoy Eying

### To the Friends and Colleagues of Bob Pettit:

Bob Pettit began his natural products research at the University of Maine in 1957. In fact my office was his first natural products lab while I was spending a sabbatical year at UCLA. When I returned I had a hard time reclaiming my office because Bob was unable to shift gears in the middle of a synthesis or separation procedure. Tenacity has always been an important ingredient in Bob's approach to practicing chemistry and for that matter everything else he does. If you go with him for a hike into the mountains you will have a real problem getting him to turn around and start back. His approach to chemistry and life has been and always will be relentless. Indeed, we can all look forward to more and better things to come from his efforts. My wife, Cindy, and I have regarded Bob and Jean among our very best friends since we first met in 1958.

Sincorer and Best Wishes, Bob blundap

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#### MY CLOSE FRIEND --- BOB PETTIT

It gives me a unique pleasure to express my best wishes to Bob on the occasion of the special Tribute Dinner sponsored by the International Foundation for Anticancer Drug Discovery. Bob and I have been friends and colleagues since our days at Wayne State University in the late 1950's! Perhaps it is appropriate to mention a few experiences in "Old Main" at that time.

The lab was better known as "cockroach heaven" and under the supervision of our Mentor, Carl Dierassi, it was necessary to observe certain precautions due to the highly restricted area available for the experiments. A normal 7-8 foot lab bench was divided by an aluminum rod "fence" into two equal 3-4 foot spaces for each individual student to perform his or her experiments. In effect, the laboratory normally suitable for 12 students, was packed with more than 20 researchers, so that neither fat nor sloppy workers were allowed. Bob had the misfortune of working next to a colleague (no name mentioned here) whose responsibility was to study the thicketalization of steroids with the highly smelly reagent, ethanedithicl. This colleague was well organized in the sense that shortly before noon of a normal working day, he would set up his experiment and then disappear for his afternoon Siesta, while those of us who worked a more normal working day, were left behind to endure the smell. The situation would turn particularly bad during the hot. humid days of the Detroit summer and with total lack of any air circulation at Old Main. A logical solution for some of us was to disappear for a "beer" to the local pub. However, Bob being a hardworking and persistent student who never agreed to the drinking of beer nor any other alcoholic beverage, would remain in the lab. In view of such exposures, I am confident that Bob's internal proteins are full of SH groups and that may explain why he remains in such outstanding physical shape!

One of the highlights of my scientific career was to be invited as a Speaker at the recent ACS Symposium on the occasion of Bob being the recipient of the Ernest Guenther Award in the Chemistry of Natural Products. This Award is only a small token of Bob's brilliant and extensive contributions in the overall field of organic chemistry, medical science and related subjects. His long standing dedication to the

development of novel anti-cancer drugs has been much appreciated by the large number of scientists who participate in this diverse and highly important area.

Bob, it my pleasure and desire to extend to you my wishes for many more years of good health and continued success in your scientific endeavours. My wishes also go to your wonderful wife Jean, and your children, who have stood by you with understanding and patience.

Finally, I deeply regret that I am unable to enjoy this Event with you and your family.

Radka also wishes to express her congratulations on your many contributions to the scientific community and for your help during her Ph.D. studies.

Cordially

Your friend forever!

Jim Kutney

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75th Anniversary Appeal Chairman Lord Mackay of Clashfern

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29 October, 1998

# To the Friends and Colleagues of Dr Bob Pettit

For many years Bob Pettit has been a great friend of the Cancer Research Campaign, a major UK cancer charity and European leader in anti-cancer drug development. He has submitted to us many interesting molecules derived from exotic sources and with equally exotic structures for consideration by our Committees. Never satisfied with conventional courier methods for sending compounds, we can always depend on Bob to arrive at our meetings with samples of materials in his pocket. (Who knows what he tells Customs?) He then has a photograph taken of him handing the material over. This is to be in readiness for when the compound turns out to be THE breakthrough in treating cancer!

Of the compounds which Bob has brought to us, and which the Cancer Research Campaign has been privileged to develop, Bryostatin 1 is showing great promise and has progressed furthest through the drug development process, with four different CRC trials complete or in progress. More recently, the impressive anti-vascular properties of Combretastatin A4 phosphate were discovered by Cancer Research Campaign scientists and should enter clinical in the UK in the very near future.

We look forward to a long and equally productive continuing collaboration with Bob for many years to come. We are sorry we cannot be with you at the dinner. Please pass on our best wishes to Bob on behalf of everyone, past and present, at the Cancer Research Campaign.

Yours sincerely

Dr Sally Burtles

Assistant Director of Drug Development (Pre-clinical)

Dr David Secher

Director of Drug Development

## WHERE Divinity, Science & Research are Undifferrentiated

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Acharan S. Narula, Ph.D. President

October 18, 1998

## To the Friends and Colleagues of Dr. G. Robert Pettit

I am so delighted to know that the International Foundation for Anticancer Drug Discovery at Phoenix, AZ will be honoring, Professor George Robert Pettit, Ph.D. Director and Dalton Professor, Cancer Research Institute, Arizona State University, Tempe, AZ, at a special tribute dinner, on November 18, 1998 for his outstanding contributions in the discovery of natural anti-cancer drugs.

Dr. Pettit is clearly an outstanding person, who has vividly demonstrated that if you focus your attention on the process of discovery, persevere the ups and downs that come your way, and leave the outcome of your efforts in the hands of the divine, success will eventually come your way. His life is a glowing example of utmost dedication. Through his research he has demonstrated that he can accomplish the impossible. And, I know the best of Dr. Pettit is still to come!

Indeed, a few days ago, I had a dream where Dr. Pettit visited a 27 years old terminally sick cancer patient, who was not responding well to any therapeutic agent. At this, I suggested that if one can make this cancer patient "laugh" at her cancer, then the cancer will become her friend and not an enemy. The patient took this recommendation to her heart, and she started laughing at her cancer for hours at a time daily. Strangely, by taking this non-toxic, infectious agent for only a few weeks, there was a total recovery of her cancer! When, I informed Dr. Pettit that the terminally sick patient is now fully recovered, he said, Acharan, Laughter is the BEST MEDICINE.

To this I said, Dr. Pettit, while we can make each other laugh, I know with your tenacity, you will one day feed cancer cells not drugs, but "LAUGHTER" and change their phenotype to normal cells.

THAT is the reason why I say, the best of Dr. Pettit is yet to come!

ATT Sizhnarula. ACHARAN S. NARULA, Ph.D.

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13 October 1998



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Ms Marcia K Horn **Executive Director** International Foundation for Anticancer Drug Discovery 27 West Morten Avenue Phoenix AZ 85021-7246 **USA** 

#### Dear Ms Horn

I would like to add my congratulations on Bob's 40 years in Cancer Research. I have collaborated with Bob in studies of the mechanisms of actions of Bryostatin 1. It has been a pleasure to work with him and I vividly recall his acute sense for the most appropriate expressions when it came to the manuscript work. Unfortunately, I can't come to the tribute dinner but I am sure it will be a very jolly and happy occasion.

Yours sincerely

Professor A Gescher

TO THE FRIENDS AND COLLEAGUES OF DR.G.ROBERT PETTIT:

It is with profound admiration for Bob Pettit and his work that I take note of his being honored by the International Foundation for Anticancer Drug Discovery. The following will remind Bob that we have a few things in common:

We both met for the first time through our contacts with Matthew Suffness, a highly professional manager of research funds at the National Cancer Institute in Bethesda. We both liked Matthew Suffness who died at the early age of 52 very much.

We both hold experiments as the essential part of scientific communication in high regard and adhere to the Ruzicka principle that good papers have a short introduction only but a long experimental part.

Last but not least: We both like good food and enjoy good wines and are for these reasons probably a little heavier than our colleagues who avoid these tidbits. With Blake's quatrain I once more express my congratulation:

To see the world in a grain of salt

And haeven in a wildflower

Hold infinity in the palm of your hand

And eternity in an hour

Arnold Brossi, Ph D. Research Professor UNC

#### To the Friends and Colleagues of Dr. Bob Pettit:

Reflecting back on one's past, one cannot help but realize how certain, special individuals have had a profound affect in influencing and shaping our lives. Dr. Pettit is certainly one of these people. I first met Dr. Pettit in 1965. He was a new, eager, aspiring professor from the University of Maine who had just joined the ASU chemistry department. I was a new graduate student. I still remember one of the first courses which Dr. Pettit taught at ASU. It introduced me to natural products chemistry. The course covered the history and chemistry of steroids. What was so unique about this course was that Dr. Pettit not only discussed the isolation, characterization and synthesis of these important compounds, but interspersed his presentation with a number of very interesting stories and anecdotes concerning the pioneer chemists in this area. Not only did he make the chemistry interesting, but his course made me realize that these were real people, with all their foibles, professional jealousies and conflicts. Sometimes they performed brilliant research leading to major discoveries; sometimes they were simply lucky, being at the right place at the right time. In any event, what I believe Dr. Pettit wanted his students to learn from this course was that we could all do important chemistry. All that was required was that we dream big dreams, strive and persist to achieve those dreams by performing good professional work, and eventually those dreams would become reality.

Over the years, my relationship with Bob gradually changed from that of a student, to that of a personal friend and associate at ASU-CRI. I came to know him as a sensitive man, with a patience to listen to one's problems and the willingness to help solve them. We would often get into some very interesting discussions, covering a wide range of topics. Sometimes we would simply be exchanging ideas concerning being a good parent, raising a family or following the progress of our respective children. Sometimes we would simply talk chemistry. Regardless of the topic, Bob provided sound advice in solving any problems encountered, both in the lab and on a personal level. For this I am very grateful.

During our discussions over the years, I also began to realize how much Bob and I had in common. One particular occasion comes to mind, which always makes me chuckle. One day we were exchanging tales of our early childhood and our then, budding interests in chemistry. In those days, introduction to chemistry involved getting your first Gilbert or Chemcraft chemistry set for birthday or Christmas. He, like myself, quickly evolved past the chemistry set stage to the bigger and better things, i.e., how to build a better pyrotechnics display with commonly obtainable chemicals. Unlike now, back in the 40's and 50's an aspiring young chemist could buy chemicals from the local chemical supply house or drug store, with no questions asked. In any event, one day Bob apparently was able to score big-time by obtaining a bottle of a very interesting chemical called titanium tetrachloride. Now for those of you who are not familiar with this chemical, it occurs as a heavy, dense liquid which must be kept in a tightly stoppered bottle. The reason for this is that upon exposure to air, the chemical decomposes rapidly, turning into a dense smoke. As a matter of fact, this compound was commonly used in smoke bombs by the military and police agencies in those days. Well, as luck would have it, while Bob was

investigating the properties of this exciting new material in his parent's basement (which he had converted into the first Pettit chemical laboratory), he accidently banged the bottle against the chemistry bench and the bottle, with all its contents, crashed to the floor. Needless to say, there were serious repercussions to be had in the Pettit household during the ensuing weeks. In any event, I gather that the family had to vacate the premises until the smoke cleared. Whether the fire department had to respond, I'm not sure. Bob would have to fill you in on these finer details. Bob also passed along many other interesting adventures during his teenage years in the laboratory, but these are best told by himself.

One, rather sad observation that we both made from this exchange of tales is that it is unfortunate that such opportunities for the free exploration of chemistry, such as we conducted back then, are no longer available to today's youth. Now, many of the tools of a chemist, such as the simple possession of a balance, flasks and certain chemicals are illegal in some states. There seems to be a pervasive fear of chemicals, a "chemophobia" if you will, that pervades our current society. I genuinely believe that such freedoms which existed in his early youth played a major role in shaping Dr. Pettit into the successful scientist he is today. Of course, in addition to his fascination with chemistry, other experiences during his early youth had a profound influence on him. Bob has recounted on numerous occasions of his first encounters with cancer victims during his youth, and the sobering effect this had on him. Since that time, he has endeavored to find a cure for this disease. I hope Bob is successful and lives to see the day when cancer is no longer a threat to society. I know that this is his dream. I also know he won't quit until his dream is realized.

Dr. Del Herald Associate Research Professor Cancer Research Institute Arizona State University

Dil Herald



#### CANCER RESEARCH INSTITUTE

G. R. PETTIT, DIRECTOR,
REGENTS PROFESSOR OF CHEMISTRY AND
DALTON PROFESSOR OF CANCER RESEARCH
AND MEDICINAL CHEMISTRY

Main Campus PO Box 872404 Tempe, AZ 85287-2404 (602) 965-3351 FACSIMILE (602) 965-8558

October 19, 1998

#### To the Friends and Colleagues of Dr. G. Robert Pettit

I have known Professor Pettit since his arrival at Arizona State University in 1965. At that time his research group numbered 17. In those early days at ASU, he was very interested in natural products chemistry and the possibility of anticancer drug activity. Graduate students and postdoctoral research associates were involved in synthesis of targets suggested by Professor Pettit. I left ASU in 1968 to 1973 and upon my return, found the research group had expanded to include a new Natural Products Group with up to a dozen undergraduate students involved in the initial extraction of marine and plant material collected from around the world for investigation of potential anticancer activity. It was in July of 1975 that the group was officially recognized as the Cancer Research Institute. Today our numbers average 55.

Over the years there have been some remarkable discoveries made from both marine and plant life. At every turn in the quest for new drugs from natural sources, there have been unexpected surprises. Fortunately due to Professor Pettit's unwavering attitude towards research, although we struggled at times, we did succeed with the discovery of new potential anticancer drugs such as the bryostatins, dolastatins, cephalostatins, and spongistatins from the sea, and the combretastatins, phyllanthoside and pancratistatin from land plants.

An example of some delays in marine material acquisition was in the recollection of the bryozoan, <u>Bugula neritina</u>. The original active specimen was found off the coast of Florida, and discovered again growing in Mexico. Upon returning to the same site in Mexico for a large scale collection, the area had been scoured by a recent hurricane and little bryozoan could be found. At this point, sites were explored along the California coast and found to have <u>Bugula</u> in relative abundance. It was from these California collections that bryostatin 1 was discovered and to date, the only area where the bryozoa produce the crystalline compound. <u>Bugula</u> from the Mexico and Florida sites yielded more complex mixtures of other bryostatins, none being suitably crystalline for x-ray analysis.

Professor Pettit's attributes of patience, a very focused approach toward anticancer drug discovery and perseverence have led to his remarkable successes. One of the major driving forces behind his quest is a basic sensitivity to the plight of cancer victims and a genuine need to alleviate human suffering with superior anticancer drugs. All of us wish him well, and those of us in the CRI have joined forces with him to accomplish his aims.

Cherry L. Herald, Ph.D.

Cherry L. Merald

Associate Director



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October 20, 1998

To the Friends and Colleagues of Bob Pettit:

Although I am unable to be with you on this momentous occasion, I would like to join you in honoring the extraordinary career of Bob Pettit.

Bob's dedication to cancer research is truly inspirational. The development of cancer chemotherapy is due in large part to the efforts of Bob and his colleagues at the NCI who pioneered in this work and demonstrated its feasibility when there was little activity in the commercial sector. The many varied and successful programs in the pharmaceutical and biotechnology industries today vindicate Bob's vision and dedication.

Congratulations Bob on this great day, and best wishes for continued success.

Sincerely,

Thomas H. Smith, Ph.D. Senior Research Scientist

13801 ¥ork Road, Apt. B-1 Cockeysville, MD 21030 October 15, 1998

Dr. G. R. Pettit Cancer Research Institute Arizona State University P. O. Box 872404 Tempe, AZ 85287-2404

Dear Bob:

-On the occasion of the IFADD Tribute Dinner Honoring you, I have been asked to join a group of colleagues commending you in writing, even though distance and health prevent me from being present on this memorable occasion.

In summarizing how you reached your present stature and and prominence in the cancer research field, I would say that some important points are a good foundation com bined with tremendous drive and high goals. You have the necessary leadership qualities and energy necessary to put together such a group as the Cancer Research Institute. You have great tenacity and a never-say-die spirit. This has been essential when times were rough and funding was difficult. I remember one period when NIH funding, for some reason, was cut off; you didn't give up, but as you put it, "passed the hat"--sought private sources of funding to tide CRI over this tough period, And you were succesful! In your place, most scientific administrators would have given up.

After years of struggle, CRI now has its own quarters--a campus building that was vacated, which was suitable, but I'm sure was coveted by other departments or groups. This is a big achievement.

And I musn't fail to mention your infectious optimism--an important part of your leadership qualities.

I don't know how the prospect of compulsory retirement may affect you--I hope it will not mean you have to give up your post. If it does, I'm sure you'll still be around--or possibly working with the diving team part of the time. Which I'm sure would be to your liking, probably more than office work.

Sincerely yours,

Cecil R. Smith

1211 Bruce Road ● Wilmington DE 19803 ● (302) 764-1714 ● e-mail RCThamm@AOL.com

#### October 6, 1998

#### To the Friends and Colleagues of Dr. G. Robert Pettit:

It is a real pleasure to learn that Bob has been accorded the well-deserved honor of a special Tribute Dinner. I wish I could be there.

I have known Bob for almost fifty years, from the time he and I toiled together as undergraduate chemistry students at Washington State College (now a proper university) and it has been my great pleasure to have him as a friend ever since. Together, we spent many hours not only in classes and laboratories, but in quiet, intense study sessions while we memorized organic structures and name reactions and learned all the other "stuff" that goes into the making of a chemist. For a time we lived together in a co-op house off-campus and also learned the art of relaxation and how to enjoy the occasional party. It was a great time in our lives.

Although we have met only once since we went our separate ways to graduate schools we have been in almost yearly contact at Christmas time. It is truly a friendship that has withstood the test of time. I'm happy and proud to say that my son, a veterinarian researcher in oncology is now collaborating with Bob in some of his clinical evaluations.

I have followed Bob's illustrious career over the years with great pleasure. His successes as a researcher and an administrator have not been surprising, in view of my memories of his intense interest in and love of chemistry, his originality, and his drive. I can only wish him continued success for as long as he may choose to follow his field.

To my friend Bob I say: I wish I could be there to join you in this gathering which has come in your honor. I applaud you and your work and treasure our friendship - past and future. May you and your family enjoy peace and good health.

Sincerely,

Richard C. Thomas (Diche)



Department of Chemistry and Biochemistry Main Campus PO Box 871604 Tempe, AZ 85287-1604

Phone: (602) 965-3461 FAX: (602) 965-2747

October 12, 1998

#### Dear Bob:

I have learned that you are to be honored at a Special Tribute Dinner by the International Foundation for Anti-Cancer Drug Discovery. With regrets I shall be unable to attend this gala affair and I take this simple means to forward my sincere compliments and congratulations on the honor to be bestowed on you. I am delighted that you continue to receive the recognition that you so richly deserve.

I remember your joining the faculty of the Department of Chemistry in 1965 from the University of Main. Since that time we have been colleagues, interacting at many levels. I still remember those early days when we all struggled to develop professionally as educators and scientists and in the process work toward making Arizona State University a Class I Research University. You certainly helped in making that goal a reality. Your dedication, perhaps one should use the word tenacity, in the isolation, characterization and synthesis of naturally occurring anti-cancer agents has been instrumental in achieving your goals. Your self-discipline, so important to all scientists in advancing knowledge, has been exceptional in its singular focus. Of course, you had fun in the process as you traveled the world, tracked through forests, scuba-dived beautiful waters and even surviving extreme temperatures and horrendous storms. Of course, those of us who have been engaged in education and research recognize the beneficence we have had from an era of abundance. But the surface of development in health and education only has been scratched and now the hard work has to begin. This will require the ingenuity and hubris you have used so far to notch up to a higher level.

In recognizing your efforts as "a knight in shining amour slaying the dragon of cancer(s)," what is overlooked all too commonly is the civility, morals and manners you have practiced so prudently over the years. We all know that progress, especially in science, in health, has been one that has been based on the efforts of so many others who have gone before us. You have recognized that indebtedness that we have in climbing on the shoulder of others and in this day of science, interdisciplinary interactions become all the more prevalent and required.

I congratulate you, I wish you many more years of success and the good health to continue enlarging our knowledge and armentaria for the benefit of society.

A tip of "ye olde' Hatlo hat" and toast to your achievements and to the future.

Warmest regards.

Sincerely,

Joseph Harris

Professor Emeritus Past Associate Chair

Department of Chemistry & Biochemistry

JH/jr

# ASSOCIATED GYNECOLOGISTS LTD. GYNECOLOGY • ONCOLOGY

WILLIAM E. CRISP, M.D.

16620 N. 40TH STREET SUITE E PHOENIX, ARIZONA 85032 PHONE (602) 992-1966 FAX (602) 992-9894

October 6, 1998

G. Robert Pettit, Ph.D. Director of Cancer Research Institute Arizona State University Tempe, AZ

Dear Bob:

It's an honor for me to add to the many plaudits that you will receive on this special night. All of them are well-deserved.

Your tenacity and genius in isolating organic nontoxic compounds from marine organisms for the control of cancer is singular and I think worthy of a Nobel Prize.

It's been my pleasure to know you on such an informal and friendly basis, your enthusiasm has been an inspiration for me personally.

Congratulations, Bob. I look forward to continuing our association during the coming years.

With kindest personal regards.

Sincerely,

William E. Crisp, M.D.

WEC:RT

College of Science Department of Chemistry



P.O. Box 210041 Tucson, Arizona 85721-0041 (520) 621-6354 FAX (520) 621-8407

September 19, 1998

#### To the Friends and Colleagues of Bob Pettit:

I am sorry not to be able to attend the Pettit Tribute Dinner, but am very pleased to be able to add this letter for the occasion, to make it clear how much Bob has helped my research group over the years.

Our work on structure determination of antitumor agents started in the 1960s when there was a program here directed by Jack Cole for finding antitumor agents in desert plants. This gave some interesting leads such as bouvardin and uvaricin. When Jack went heavily into administration, we lost our supply of antitumor agents from natural sources.

Bob helped us out by providing some fascinating structures on which they had done most of the work, and introduced us to what are currently the most powerful NMR techniques for structure determination: HMQC and HMBC. We helped to finish off some eight structures in collaboration with their group.

At our request, they also very kindly provided us with some important target molecules for synthesis: axinastatin 4 and dolastatin 11. Our syntheses of these molecules are now published, and our main current research effort (supported by the NIH) is to make simpler and more effective analogues of the latter.

Two of my former students have had the pleasure of working in Bob's group: Dennis Doubek and Stuart Taylor. Dennis, an undergraduate researcher with me, has been a mainstay of Bob's isolation efforts for many years. Stuart did undergraduate research with Bob, earned a Ph.D. with me, and then returned to Bob for postdoctoral work.

There is no question that (with the possible exception of Jack Cole many years ago), Bob has helped my research group far more than anyone else has. He has been kind enough to find time to help us in addition to all of the outstanding work in his own group, and I am glad to have this opportunity to thank him publicly in this way.

I am sure you will have a delightful dinner.

Sincerely,

Robert B. Bates

Professor

Marinus. W. Lobbezoo, Ph.D.
Rietmeent 3
NL-1218 AV Hilversum
Phone: 035-691 0052
Fax: 035-691 0036

Email: lobbezoo@euronet.nl

October 1998

To the Friends and Colleagues of Dr. Bob Pettit,

The first thing I ever learned about our friend and colleague Bob Pettit was that he and his coworkers had prepared a synthetic compound, named DABIS perchlorate, having broad antitumor activity in laboratory tests. This was in de mid 1980s when I first became involved in European cancer drug development. His compound had an interesting profile and generated our interest at the EORTC New Drug Development Office in Amsterdam. However, when we requested supply of this compound for further testing in Europe, we learned that it could not be shipped by air because it was ... EXPLOSIVE! I did not know Bob Pettit personally yet at that time, but you can imagine that I began to think about him as a possibly violent person with whom I might better not become involved any further.

However, when I met Bob for the first time a little later, I found out that my initial thoughts about him were entirely wrong. I got to know Bob Pettit as a very kind and gentle person, an excellent medicinal chemist, someone with an absolute dedication to tackling the cancer problem. Of course, he had already realized that DABIS perchlorate was an explosive compound. He had prepared an analogous compound, named DABIS maleate, which was not explosive and had retained all the favorable antitumor properties of DABIS perchlorate. We embarked on the development of DABIS maleate in Europe and this was the reason for many further contacts with Bob Pettit.

Now, after more than ten years of friendship with Bob, I fully support the initiative of the Pettit Tribute Dinner to honor the man whose great scientific creativity and personal dedication have made a difference to the prospect of cancer treatment. I congratulate all of you who collaborating with him on a daily basis in a – probably unprecedented – effort to isolate and characterize (very complex) natural antitumor compounds, and all of you providing him the supportive environment he deserves so much. Keep the good work going!

Yours sincerely,

Marinus W. Lobbezoo, Ph.D.

Medicinal chemist

Former director EORTC New Drug Development Office

#### DONALD J. ULRICH, JR.

September 23, 1998

Dr. G. Robert Pettit
Director
Arizona State University Cancer Research Institute
Arizona State University
P.O. Box 872404
Tempe, Arizona 85287-2404

Dear Bob,

It has been a long trip since our meeting in the old Bret Hills neighborhood.

We will never forget the dedication with which you pursued the goals that are now becoming reality.

Even in those early tough years, you were convinced if you could save the Institute financially, you could make major contributions to the cures for cancer.

We are proud to have been of assistance in those early days of financial peril.

We have watched your progress with pride and feel, in some small way, a part of the good you are doing for mankind.

Congratulations and God speed.

Régards,

Don and Sharon

7530 NORTH SHADOW MOUNTAIN ROAD
PARADISE VALLEY, ARIZONA 85253
PHONE 602 • 368 • 8975
FAX 602 • 368 • 8976



National Institutes of Health National Cancer Institute Technology Development & Commercialization Branch NCI-FCRDC, PO BOX B Fairview Center, Suite 502 Frederick, MD 21702-1201 (301) 846-5465 (301) 846-6820 fax

October 16, 1998

To the Friends and Colleagues of Dr. G. Robert Pettit:

I wish to join you all in honoring the chemist who I consider one of the most celebrated "Renaissance" chemists I have ever known. I became acquainted with Dr. Pettit from 1987-1992 when I was the chemistry representative for the anti-RNA-viral drug development program directed by the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick, Frederick, Maryland. The enthusiasm demonstrated by Dr. Pettit was highly contagious to me. His idealism in developing potential therapeutic agents for diseases which would not lend themselves to study by the pharmaceutical industry was also inspiring and equally contagious. The remarkable in vivo efficacies (100% survival in treated, infected mice cf. to 100% mortality in controls) demonstrated by pancratistatin and several synthetic and naturally-occurring analogs were the subject of manuscripts and seminars which evoked a great deal of enthusiasm from readers and audiences. It is unfortunate that the program had to be curtailed for budgetary reasons.

I especially enjoyed our research meeting visits since Bob's timetable for meetings later in the day suited my biological clock perfectly. In addition, as a prostate cancer survivor, I have come to appreciate his concern and compassion. God has gifted Bob Pettit uniquely and Bob continues to respond by using his gifts to the maximum.

With warmest congratulations,

Bjarne Gabrielsen ("B.J.")

Technology Development & Commercialization Branch

NCI-FCRDC

Frederick, Maryland



# The School of Pharmacy

University of London

**Centre for Polymer Therapeutics** 

Head of Centre:

Professor R Duncan, BSc, PhD Telephone: ++44 (0) 171 753 5932

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T A Connors Honorary Professor Phone 0171 753 5934 Fax 0171 753 5931 E-mail tconnors@cua.ulsop.ac.uk

15/09/98

# To the Friends and Colleagues of Bob Pettit

It is a great pleasure to have been asked to write a few words on the occasion of the Tribute Dinner organised by the IFADD to mark Bob's fortieth year in cancer research.

Bob and I have been colleagues and friends for more years than I care to remember. Our friendship certainly goes back to the late 1960's when we were both on the Board of Counsellors of the NCI. I have one reason to be extremely grateful to Bob. In the 1970's I made a great fuss about cancer research money being wasted on extensive preclinical toxicology. There was plenty of clinical evidence that all that was required was a simple study involving only rodents, to obtain the safe dose at which to begin the trials. With Brian Fox, his late boss Laszlo Lajhta and with plenty of advice from people such as Omar Yoder, we set out a plan for carrying out simple toxicology studies for anticancer agents which would be one tenth the cost and carried out in a quarter of the time . Nobody was prepared to fund such a project until one year the Cancer Research Campaign found itself in the unusual situation of having more money than they had projects to fund. To our surprise. Brian and I were given £100 000 for five years to develop our ideas. At this point one realises that theory may be quite different from actual practice. We had stated quite clearly that the scheme would be used to develop the ideas of academics. Unfortunately it became clear to us that there were no more than half a dozen really interesting drugs developed by academics in the previous years and that after one year the Committee would become redundant. Then along came our saviour, Bob. He asked the Committee to consider developing, Pettit's mustard, pancratastatin, dolostatins 10 and 15, bryostatin, combretatstain A4 and a host of other extremely interesting novel chemicals. Many of these have now had clinical trials and a combretatstatin prodrug might well develop into one on the most interesting anticancer drugs of the decade. As a result of Bob's input, the Committee became well established and now works with the European and American drug development committees to introduce new classes of agent to the clinic. It is marvellous for students and established researchers alike to hear Bob lecture on how he discovers new agents. Starting from scuba diving in tropical islands and collecting exotic marine organisms, through screening and identification followed by total chemical synthesis Bob directs it all with skill and I am sure has encouraged many a young student to enter the field.

Bob's knowledge of chemistry is also legendary. I remember once when a venture capital company paid a visit to the CRC and presented their wonder drug. Bob immediately recognised the structure as Krebiozen an unproven method of treatment, which like Laetrile had a brief burst of publicity as a cancer cure all. Krebiozen was in fashion way back in the 1950's so many scientists, who believe that anticancer agents did not exist until the advent of the computer, did not have the structure in their



# The School of Pharmacy

University of London

#### **Centre for Polymer Therapeutics**

Head of Centre:

Professor R Duncan, BSc, PhD Telephone: ++44 (0) 171 753 5932

Fax: ++44 (0) 171 753 5931 E-Mail: ruduncan@ulsop.ac.uk

reference base. The meeting with the venture capital company was very brief after Bob's comment and we did not hear of them again

It is always a pleasure to meet Bob at scientific meetings all over the world. Most meetings have more than one dinner where the wine flows freely and often some delegates become somewhat noisy and boisterous. This was never the case with Bob in my experience and certainly in my case he seemed to be the person who ensured that I and some of my other noisy colleagues got back to our hotels. However I do have a memory of an EORTC/NCI meeting in Amsterdam. After the conference dinner Stan McElhinney from Dublin found a piano from somewhere or other and Patrick Creaven from Buffalo conducted the delegates in loud and untuneful singing. I am sure Bob joined in and was a loud and as boisterous as anybody. Unfortunately I cannot find a photograph I once had which proves my point, but if I ever find it I will forward it for late inclusion in the Tribute Journal.

I am pleased that I have known you as a friend and colleague Bob and enjoy yourself at the dinner.

Tom Connors

# UNIVERSITY of PENNSYLVANIA

Department of Chemistry Philadelphia, PA 19104-6323

Amos B. Smith, III

Rhodes-Thompson Professor of Chemistry
215-898-2440 (Voice)
215-898-5129 (Fax)
smith@a.chem.upenn.edu

September 17, 1998

Professor G. R. Pettit
Director, Regents Professor of Chemistry
and Dalton Professor of Cancer Research
and Medicinal Chemistry
Cancer Research Institute
Arizona State University
P. O. Box 871604
Tempe, AZ 85287-1604

Dear Bob:

I write to solute and to congratulate you on this most festive occasion, A Tribute Dinner sponsored by the International Foundation for Anticancer Drug Discovery. Your contributions during the past 40 years are legend in the worlds conquest against cancer and related disease. Indeed, I can think of no one in the chemical or medical arenas more worthy of such recognition. Equally important has been your leadership, counsel and friendship to all of those in academia, government and industry who share your interest in combating cancer. From a personal perspective, you have always been exceedingly generous with your support of our program here at the University of Pennsylvania, and I am deeply appreciative of your help. I, of course, look forward to many additional years of collaboration with you and your Research Group at Arizona State University.

In closing, please have a most wonderful and festive day.

Best personal regards.

Sincerely yours,

Amos B. Smith, III

ABS:daw



# भारतीय रासायनिक जीवविज्ञान संस्थान

### INDIAN INSTITUTE OF CHEMICAL BIOLOGY

(COUNCIL OF SCIENTIFIC & INDUSTRIAL RESEARCH)

**Prof. U. R. Ghatak**, F.A. Sc., F.N.A. INSA Senior Scientist

Jadavpur Calcutta-700 032 India

D.O. No. URG/9/25(i)/98

Date September 25

# To the Friends and Colleagues of Dr.G.Robert Pettit

Although physically on the other side of the globe on this colorful evening, I am deeply gratified to have this opportunity to join you in wishing my sincere congratulations and hearty wishes to **Bob Pettit** on the occasion of this special Tribute Dinner honoring his long and impressive years in cancer research.

I still remember fondly how **Dr.Pettit** befriended a young Indian Postdoctoral Research Assistant of nearly same age as his, on his first arrival to a snow white campus of the University of Maine, Orono, on an early January day, 1960, after a long trip through Europe by boat from the warm tropical Calcutta weather. As I recall, there were three other Postdoctoral Assistants in his group, two from Liverpool and one from Bangalore, who joined few months earlier. **Bob** had nearly half a dozen of graduate students. Several projects on transformation of steroids and triterpenoids, synthesis of cancerocidal agents and general organic synthesis were being actively pursued. I was engaged with the isolation and chemical studies of triterpenoids and alkaloids from various species of *Labiatae*. This was expanded to a very useful study of a new synthetic procedure for the direct reduction of lactones to cyclic ethers developed in that laboratory.

We spent together many hours in discussing the problems. Quite often he used to invite for dinner at his home. Aside from high standard and remarkable research output, **Dr.Pettit** trained large number of graduate students and Postdoctoral Associates, many of whom were from abroad. His strong determination in conjunction with the demand for nothing less than excellence has been a model for me for my long research career. After a highly rewarding year at Maine I shifted to the University of California, Berkeley. We met several times at Orono and New York in the later years and remained a good friend throughout.

I wish **Bob** a good health, many further scientific successes and particularly to be always as he is now; the great person and the great scientist.

Yours Msha Repractate

(U.R.GHATAK)

# GRIFFITH UNIVERSITY



Queensland Pharmaceutical Research Institute

Cnr Don Young Rd & Forest Court Mt Gravatt Research Park Nathan Brisbane

Tel:

+ 61 7 3849 1366

Fax: Email:

+ 61 7 3849 1292 M.Butler@qpri.gu.edu.au

11 October 1998

Dear Dr. Pettit,

I am writing to you to convey my warmest regards and congratulations on the occasion of your Tribute Dinner from the International Foundation for Anticancer Drug Discovery.

Your sustained and unwavering attack on the cancer from the natural products tact is almost unprecedented. The thing I admire so much about your work is how you and your group takes a project to the final stage no matter what the effort. The reward is there plain to see in the bryostatins and dolastatins to name a few. I remember one day at CRI asking you why you didn't use the extracts more for other disease targets. I got one of your serious faces and you said "Not until we've beaten cancer Mark!".

My 18 months at CRI in 1993 and 1994 was some of the best times of my life. Not only was the natural products work stimulating and rewarding but also for the chance to meet so many great people at CRI and to live in Arizona. What a great place to live! The international flavour of the research group has also rewarded me with so many friendships that continue despite the distances involved. It's a pity I had to move on so quickly but good jobs in Australia are hard to come by!

I look forward to seeing you in the near future.....

Yours sincerely

Dr. Mark Butler

To the Friends and Colleagues of Professor Bob Pettit:

I would first like to express my heartfelt congratulations to Dr. Pettit for all of his achievements in the field of anticancer natural products drug discovery over the past several years. I am unable to be present for the IFAAD awards dinner at the Arizona Biltmore. However, I do wish to write a letter on reflections of my experience at ASU-CRI.

I am very grateful to Professor Pettit and his colleagues for providing me with valuable training and experience in natural products isolation, and in particular, the bioassay guided fractionation of antitumor active marine natural product extracts. Upon receiving my PhD degree in the phytochemical investigation of alkaloid containing plants, I was offered a post-doctoral appointment with Prof. Pettit in June 1983. At ASU-CRI, I learned not only a vast array of isolation methodology, but also learned for the first time how to interpret cancer cell line bioassay results to guide a series of separations to the active anticancer compound. I experienced nearly all phases of a separation problem, starting with a crude marine extract, followed by brilliantly colored Sephadex LH-20 columns, and finally to some very promising purified anticancer compounds, such as the bryostatins and halichondrins. There was always a sense of mission to the work at ASU-CRI. The mission, that is to find new naturally occurring compounds for the treatment of cancer, was a powerful motivator. Dr. Pettit impressed me with his boundless optimism and dedication to finding a cure for cancer. I am very proud to have had the opportunity to work towards these goals under his guidance. The experience of mission oriented research in addition to superb technical training provided me with an excellent foundation for my current position at Bristol-Myers Squibb Company as a Senior Research Investigator in the natural products chemistry department, where I have served for the last 12 years.

I also appreciated that Dr. Pettit believed in the importance of living a balanced life, and having a sense of humor. I remember our group meetings, where in addition to normal business, Dr. Pettit would entertain the group with slide shows of his collecting trips in the South Pacific, and tales of his run-ins with sharks and marine crocodiles! Outside of work, he would often take the research group on hiking trips throughout Arizona. I will always remember one such "Symposium in the Wilderness" when he took us to Thunder River trail at the north rim of the Grand Canyon. I remember discussing research results and ideas with him into the wee hours of the night.

To Professor Pettit and my colleagues (Cherry and Del Herald, Gordon Cragg, Sheobux Singh, Dennis Doubek, Yoshi Kamano, and many others), I thank you all for playing a very important role in my professional development as a natural products chemist. To Professor Pettit, I congratulate you for the IFAAD award and indeed wish you continued success in the many years to come.

Best wishes,

John E. Leet

John E- Lest

JOHN SHADEGG

REPUBLICAN POLICY COMMITTEE SOPHOMORE CLASS REPRESENTATIVE

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# Congress of the United States

House of Representatives Washington, DC 20515-0504

November 18, 1998

COMMITTEES: BUDGET

RESOURCES

SUBCOMMITTEES:

WATER AND POWER RESOURCES
NATIONAL PARKS AND PUBLIC LANDS

GOVERNMENT REFORM AND OVERSIGHT

SUBCOMMITTEES:

NATIONAL ECONOMIC GROWTH, NATURAL RESOURCES AND REGULATORY AFFAIRS NATIONAL SECURITY, INTERNATIONAL AFFAIRS, AND CRIMINAL JUSTICE

Dr. G. Robert Pettit Founder and Director Arizona State University Cancer Research Institute Tempe, AZ 85257

Dear Robert:

Congratulations on the anniversary of your 41st year as a pioneer in anticancer drug discovery. Having you here in Arizona at Arizona State University as the founder of the Cancer Research Institute makes us doubly proud of you.

Most importantly, your continuing and tireless search for the cure for cancer, searching the world for just the right marine plants and microorganisms to continue to isolate the potent anticancer compounds, is no small feat and deserves our commendation.

My family, and many others, has been affected by cancer. My desire is that in our lifetime the Dr. Robert Pettit's of the world will be able to shout out the words, "I found the cure for cancer!!!" for all to hear. That will be a most happy day.

Sorry I could not be with you this evening. We are in Washington, D. C. preparing for the 106th Congress. But, please know that I will continue to do all I can to continue to spread the word of the outstanding job you are doing. And, I pledge to join you in continuing to fight this "War on Cancer."

Sincerely,

John Shadegg

Member of Congress

JS/pjc



College of Medicine P.O. Box 245024 Tucson, Arizona 85724-5024 FAX (520) 626-6292

October 15, 1998

Marcia Horn International Foundation for Anticancer Drug Discovery 27 West Martin Ave. Phoenix, AZ 85021

Dear Marcia

Thank you for sending me an invitation to the November 18 dinner honoring Dr. Pettit. Unfortunately, I will not be able to attend this event due to a schedule conflict. Please give Dr. Pettit by regards and tell him that I am sorry I have to miss this celebration.

I was not aware that the IFADD held an event honoring cancer researchers involved in drug discovery. I would be happy to meet with you and members of your board to discuss researchers from the Arizona Cancer Center that are worthy of such honor. As you are aware, we have an internationally recognized drug discovery program here, and for more than two decades have played a critical role in developing many of the drugs that are now considered standard care in oncology today.

I appreciate your note expressing your willingness to support the efforts of Senator Ann Day in her attempt to draft legislation that would mandate managed care coverage for clinical trials. The legislation is currently being drafted and as soon as we have a copy, I will forward one on to you. We will certainly need the support of many to see this legislation through. Good luck with your event.

Best Regards,

Sydney E. Salmon, M.D.

Regents Professor of Medicine Director, Arizona Cancer Center

# STANFORD UNIVERSITY DEPARTMENT OF CHEMISTRY STANFORD, CALIFORNIA 94305-5080

PAUL A. WENDER Francis W. Bergstrom Professor

PHONE: 650-723-0208 FAX: 650-725-0259 WENDERP@LELAND.STANFORD.EDU

October 20, 1998

Professor George R. Pettit Cancer Research Institute Arizona State University Tempe, Arizona 85287-2404

Dear Bob:

I am delighted to learn of the IFADD dinner in your honor. It is a well-deserved tribute to a person who epitomizes the research scientist. You have done so much with so little over the years, introducing new chemical and clinical strategies and tools for addressing one of the most difficult problems of our time, cancer. Your work has inspired other scientists to push forward in this and many other areas. It has also made abundantly clear the great return to our society that is possible through an investment in science and higher education.

I have enjoyed our collaborations over the past decade and look forward to furthering our efforts in the years to come. I have attached a reprint of our most recent collaborative product published in the Proceedings of the National Academy of Science. It is one of many examples of your influence on science and the product of an effort that you initiated in 1968! Anyone who has explored our marine environment knows what a rich resource it is. While the marine world has I am sure been a lonely place during many of your dives, it is evident that you have carried us all intellectually into this remarkable new world. We have benefitted enormously from your pioneering spirit and deeds.

With best wishes from your friends at Stanford,

Sincerely,

Paul A. Wender

PW:lhl Enclosure



October 23, 1998

To the Friends and Colleagues of Dr. Bob Pettit:

We were at the Cancer Research Institute with Dr. Bob Pettit in the mid-eighties (1983-1989 for SBS, and 1986-1988 for CD). We joined CRI from foreign lands (India and Canada) and were pleasantly surprised by life in Arizona, and the infrastructure Bob had created. The biggest surprise to both of us was the uniqueness of Bob's character.

Bob is a very warm individual and always ensured the well being of his colleagues and family members. He amazed everyone with his colossal physical endurance, leaving many of us far behind on hiking trails. Some of the best times we spent together were on hiking trails, after we caught up with him, sitting on a rock, enjoying a half a dozen chocolate bars. His sweet tooth was probably the source of his extra energy. The only problem Bob encountered on the trails is the lack of ice cream vendors to satisfy his gigantic ice cream craving.

Of all the individuals we have met over our careers, none is more perseverant and persistent than Bob in pursuing and accomplishing his objectives. We could not appreciate this quality at our immature stage, but in hindsight are now very much impressed by Bob's qualities.

We were involved with several major discoveries at the time, which include dolastatins, combretastatins, and cephalostatins. Bob made great efforts to insure that the Institute was always well equipped. This would ensure the best possible productivity from his group members. In spite of the inevitable staff turnover rate of an academic setting, Bob could always recruit good people to carry on his quest.

His achievement of bringing so many compounds to clinical trials is truly remarkable. Knowing Bob, he will not give up until most are marketed anticancer drugs.

Congratulations and Many Cheers!!!

Sheo B. Singh

Claude Dufresne

In Christ, Light

To the Friends and Colleagues of Dr. G. Robert Pettit:

Do you know someone who has dedicated their entire life to helping others? Someone who has never wavered in their resolve to not only accomplish personal goals, but goals held important by society? Do you know someone who runs several miles each day and then eats ice cream? I have had the honor of knowing such a remarkable individual. Dr. G. Robert Pettit was my graduate advisor at Arizona State University. The first time I met Dr. Pettit, he had a television crew wait outside his office while he took time to interview with me. I had never met someone so dedicated to cancer research and he immediately gained my respect.

Dr. Pettit has the kindest demeanor. It takes only a few minutes of conversation with him to realize that his commitment to cancer research is genuine. So often, a researcher looses sight of the ultimate goal when involved so intimately in the day to day science. Dr. Pettit has never lost sight of the ultimate reason he presses on against all obstacles: to help those suffering from this terrible disease. He is truly a warrior waging a long and difficult battle against cancer. Yet, through all of the struggle, Dr. Pettit never looses hope. He always believes a new drug is around the corner just waiting to be discovered. So he presses on, tirelessly, searching for the new cures from nature.

It would be unfair to speak of Dr. Pettit's success without also acknowledging the support he receives from his family. His wife, Jean, has always stood by his side in support. She helped raise their children, has helped out in expeditions, and even hosted parties for the Institute. Jean certainly deserves a thank you for all of the help she provides Dr. Pettit. It would be difficult for an individual to accomplish all Dr. Pettit has accomplished without the support of a loving family.

Let me join the International Foundation for Anticancer Drug Discovery in congratulating Dr. Pettit for 40 years of drug discovery. Let me also add a thank you to the Pettit family for all of their support and love they provide that allows Dr. Pettit to press on to the ultimate research goal. Cheers to you, Dr. Pettit and Jean! Best wishes for another 40.

Sincerely,

Duah W. Coffman

Dr. Terah W. Coffman, Chair Department of Science & Math. Warner Pacific College Portland, Oregon 97215