Ludwig Institute for Cancer Research Ltd, Zurich

Report of the Statutory Auditor on the Consolidated Financial Statements to the General Meeting of Shareholders

Consolidated Financial Statements 2018

KPMG AG
Zurich, May 24, 2019

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Report of the Statutory Auditor to the General Meeting of Shareholders of

Ludwig Institute for Cancer Research Ltd, Zurich

Report of the Statutory Auditor on the Consolidated Financial Statements

As statutory auditor, we have audited the accompanying consolidated financial statements of Ludwig Institute for Cancer Research Ltd, which comprise the balance sheet, statement of income and expenditure, statement of cash flows, statement of capital changes and notes for the year ended December 31, 2018.

Board of Directors' Responsibility
The board of directors is responsible for the preparation of the consolidated financial statements in accordance with Swiss GAAP FER and the requirements of Swiss law. This responsibility includes designing, implementing and maintaining an internal control system relevant to the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error. The board of directors is further responsible for selecting and applying appropriate accounting policies and making accounting estimates that are reasonable in the circumstances.

Auditor's Responsibility
Our responsibility is to express an opinion on these consolidated financial statements based on our audit. We conducted our audit in accordance with Swiss law and Swiss Auditing Standards. Those standards require that we plan and perform the audit to obtain reasonable assurance whether the consolidated financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the consolidated financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the consolidated financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers the internal control system relevant to the entity's preparation of the consolidated financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control system. An audit also includes evaluating the appropriateness of the accounting policies used and the reasonableness of accounting estimates made, as well as evaluating the overall presentation of the consolidated financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion
In our opinion, the consolidated financial statements for the year ended December 31, 2018 give a true and fair view of the financial position, the results of operations and the cash flows in accordance with Swiss GAAP FER and comply with Swiss law.

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EXPERTsuisse Certified Company

Report on Other Legal Requirements

We confirm that we meet the legal requirements on licensing according to the Auditor Oversight Act (AOA) and independence (article 728 CO) and that there are no circumstances incompatible with our independence.

In accordance with article 728a paragraph 1 item 3 CO and Swiss Auditing Standard 890, we confirm that an internal control system exists, which has been designed for the preparation of consolidated financial statements according to the instructions of the board of directors.

We recommend that the consolidated financial statements submitted to you be approved.

KPMG AG

Martin Schaad
Licensed Audit Expert
Auditor in Charge

Ludwig Weinschrod
Licensed Audit Expert

Zurich, May 24, 2019

Enclosures:
- Consolidated financial statements (balance sheet, statement of income and expenditure, statement of cash flows, statement of capital changes and notes)

CONSOLIDATED BALANCE SHEET AS AT DECEMBER 31, 2018

	Notes	USD 2018	USD 2017
Assets			
Cash and cash equivalents	2, 3	27,790,788	45,112,645
Financial assets	2, 4, 9	1,394,772,956	1,482,618,201
Trade receivables		97,054	167,448
External funding receivables	2	2,639,711	2,702,030
Other short-term receivables	5, 12	4,842,810	5,570,247
Prepaid expenses and accrued income		1,612,170	2,809,927
Total current assets		**1,431,755,489**	**1,538,980,498**
Financial assets	2, 6	14,899,270	14,074,266
Investments	2, 7	527	7,159,744
Net deferred tax assets	2, 18	3,277,175	2,877,301
Leasehold improvements, equipment & other assets	2	45,635	62,915
Total non-current assets		**18,222,607**	**24,174,226**
Total assets		**1,449,978,096**	**1,563,154,724**
Liabilities			
Short-term accounts payable		4,123,993	6,928,492
Other short-term liabilities	9, 11	1,477,619	1,479,138
Short-term provisions	12	3,121,794	3,233,568
Accrued short-term expenses		6,176,424	4,563,955
Deferred income	2, 13	14,582,841	16,778,023
Total short-term liabilities		**29,482,671**	**32,983,176**
Other long-term liabilities	14	1,508,017	1,429,226
Long-term provisions	15	9,708,756	8,981,685
Accrued long-term expenses		0	11,553
Total long-term liabilities		**11,216,773**	**10,422,464**
Total liabilities		**40,699,444**	**43,405,640**
Shareholders' equity			
Share capital	1	49,618	50,592
Donated capital	1	572,000,000	572,000,000
General legal retained surplus	1	9,924	10,118
Voluntary retained surplus	1	837,219,110	947,688,374
Total shareholders' equity		**1,409,278,652**	**1,519,749,084**
Total liabilities and shareholders' equity		**1,449,978,096**	**1,563,154,724**

CONSOLIDATED STATEMENT OF INCOME AND EXPENDITURE FOR THE YEAR ENDED DECEMBER 31, 2018

	Notes	USD 2018	USD 2017
Operating income			
Contributions, dividends & interest income	2	4,688,373	4,945,960
External funding	2, 13	20,959,067	31,737,969
License fees and royalties		2,537,437	4,465,281
Other operating income	8	127,806	118,656
Total operating income		**28,312,683**	**41,267,866**
Operating expenses			
Salaries and social benefits	10, 16	39,264,816	43,482,881
Laboratory supplies		6,346,110	8,093,088
Equipment and leasehold improvements	2, 8	994,884	1,736,101
Clinical trial studies		4,072,296	5,651,182
Core collaborative research programs	20	18,748,194	18,501,535
Other collaborative research programs	20	7,600,375	6,991,802
Occupancy		4,952,863	5,785,500
Travel, conferences and seminars		917,078	1,404,362
Professional fees and services		5,807,957	7,165,073
Patent and inventors' costs		948,137	1,241,060
Depreciation	2	27,813	34,878
Other operating expenses		2,241,446	2,931,704
Total operating expenses		**91,921,969**	**103,019,166**
Other items			
Loss from change in accounting for investments	6, 7	(5,590,965)	0
Share of operational loss & capital items in associated entity	6, 7	0	(4,446,338)
Gain on foreign exchange	9	1,238,436	3,620,780
Loss on foreign exchange	4, 9	(1,735,893)	(1,527,036)
Gain on financial assets & investments	2	155,091,097	296,519,130
Loss on financial assets & investments	2	(198,135,912)	(43,486,526)
Extraordinary income / (expense)	12, 17	0	667,445
Total other items		**(49,133,237)**	**251,347,455**
(Deficit) / Surplus for the year before taxes		(112,742,523)	189,596,155
Taxes			
Current income tax expense	2, 18	(158,762)	(1,289,861)
Deferred income tax income / (expense)	2, 18	236,838	(721,746)
Total taxes		**78,076**	**(2,011,607)**
Retained surplus			
(Deficit) / Surplus for the year after taxes		(112,664,447)	187,584,748
Voluntary retained surplus at the beginning of the year		947,688,374	759,164,507
Net change in restricted funds	2, 13	2,195,183	939,119
Voluntary retained surplus at the end of the year		**837,219,110**	**947,688,374**

CONSOLIDATED STATEMENT OF CASH FLOWS FOR THE YEAR ENDED DECEMBER 31, 2018

	Notes	USD 2018	USD 2017
Operating activities			
(Deficit) /Surplus for the year after taxes		(112,664,447)	187,584,748
Net change in restricted funds	13	2,195,183	939,119
Adjustments for non-cash items			
Loss from change in accounting for investments	6, 7	7,159,216	0
Share of operational loss & capital items of equity-accounted investees	6, 7	0	4,446,338
Net (loss) / gains on financial assets		42,484,358	(253,032,604)
Deferred tax changes	2, 18	(399,874)	1,628,366
Forex (loss) / gain on cash & cash equivalents		723,986	(387,639)
Other (income) / expense items		(4,480)	(1,519,993)
Depreciation	2	27,813	34,878
Other movements in operating assets and liabilities			
Increase / (decrease) in provisions		615,297	(1,505,027)
(Increase) in non-current financial assets		(1,630,584)	(307,909)
Decrease / (Increase) in receivables		860,150	(895,496)
Decrease in prepayments & accrued income		1,197,758	1,019,150
(Decrease) / Increase in current liabilities		(2,906,136)	3,939,555
(Decrease) in accrued liabilities & deferred income		(582,713)	(4,884,917)
Increase in long-term liabilities & long-term accrued expenses		167,356	306,852
Cash flow from operating activities		**(62,757,117)**	**(62,634,579)**
Investing activities			
Investment in tangible fixed assets	2	(10,533)	(12,805)
Investment in financial assets		(530,555,042)	(493,631,405)
Sale of financial assets		576,724,821	560,475,677
Cash flow from investing activities		**46,159,246**	**66,831,467**
Net cash (outflow) / inflow		**(16,597,871)**	**4,196,888**
Cash & cash equivalents at January 1		45,112,645	40,528,118
Forex effect on cash & cash equivalents		(723,986)	387,639
Net cash (outflow) / inflow		(16,597,871)	4,196,888
Cash & cash equivalents at December 31		**27,790,788**	**45,112,645**

CONSOLIDATED STATEMENT OF CAPITAL CHANGES FOR THE YEAR ENDED DECEMBER 31, 2018

Shareholders' equity

The share capital consists of 50 fully paid shares of nominal value CHF 1,000 each. The shareholders do not have any interest in the assets or income of the Ludwig Institute for Cancer Research Ltd. Their sole power is to exercise their voting rights in accordance with the exclusively charitable and scientific purposes of the Institute.

USD	Share Capital	General legal retained surplus	Donated capital	Voluntary retained surplus	Translation adjustment	Shareholders' equity
Balance at December 31, 2016	48,501	9,700	572,000,000	759,164,507	(98,103)	1,331,124,605
Surplus for the year	0	0	0	187,584,748	0	187,584,748
Translation adjustment	2,091	418	0	0	98,103	100,612
Net change in restricted funds	0	0	0	939,119	0	939,119
Balance at December 31, 2017	**50,592**	**10,118**	**572,000,000**	**947,688,374**	**0**	**1,519,749,084**
(Deficit) / Surplus for the year	0	0	0	(112,664,447)	0	(112,664,447)
Translation adjustment	(974)	(194)	0	0	0	(1,168)
Net change in restricted funds	0	0	0	2,195,183	0	2,195,183
Balance at December 31, 2018	**49,618**	**9,924**	**572,000,000**	**837,219,110**	**0**	**1,409,278,652**

Donated capital

Universe Tankships, Inc. made the following donations to LICR Fund, Inc.:

	Year	USD Amount
Initial donation	1990	500,000,000
Second donation	1991	24,000,000
Third donation	1992	48,000,000
Total		**572,000,000**

Voluntary retained surplus

The Statutes of the Ludwig Institute for Cancer Research Ltd stipulate that the surplus for the year is not to be distributed to shareholders and accordingly the available voluntary retained surplus is carried forward.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS AS AT DECEMBER 31, 2018

1. Accounting principles and scope of consolidation

Basis of presentation

The accompanying consolidated financial statements of the Ludwig Institute for Cancer Research Ltd (the Institute) are presented in accordance with generally accepted accounting principles in Switzerland (Financial Reporting Standards - Swiss GAAP FER).

Scope of consolidation

The consolidated financial statements include the financial results of the Institute, a not-for-profit organization incorporated in Zurich, Switzerland, LICR Fund, Inc. (the Fund), a not-for-profit membership corporation incorporated in Delaware, U.S.A, which was established to receive, hold and invest funds on behalf of the Institute and which is effectively controlled by the Institute, and Universe Tankships, Inc. (UTI), a Marshall Islands corporation, which is a wholly-owned subsidiary of the Institute.

All inter-company transactions and balances have been eliminated. No minority interests exist for either the Fund or UTI.

Ludwig Technologies, Inc., a Delaware, USA corporation wholly-owned subsidiary of the Institute, has been accounted for at acquisition cost. Similarly, investments of insignificant value or negative equity, in which the Institute holds at least 20% but not more than 50%, have been accounted for at acquisition cost and, if applicable, adjusted for impairment losses.

In 2017, iTeos Therapeutics SA (iTeos), Ottignies-Louvain-La-Neuve, Belgium, in which the Institute owned 37.22% of the shares and of the voting rights, was accounted for using the equity method. Due to a financing round in iTeos during 2018, the Institute's ownership interest in iTeos dropped below 20% and iTeos is not in consolidation scope anymore at December 31, 2018 but instead accounted for at acquisition cost as a non-current financial asset.

Nature of operations

The Institute carries out its scientific and clinical activities at various branches in conjunction with hospitals in university medical centres. During 2018 the Institute's research branches were situated in Brussels, Lausanne, Oxford, San Diego and Stockholm. In addition, administrative offices were maintained in New York and Zurich. The Institute has a broadly based research program that addresses the challenge of cancer using the disciplines of cell biology, genetics, immunology, molecular biology and virology.

2. Accounting policies and valuation standards

Reclassification 2017 figures

During 2018, accounting procedures and the chart of accounts were slightly adjusted in the course of the SAP byDesign implementation. As a result disclosures for balance sheet and the statement of income and expenditure have been slightly adjusted. Where necessary, 2017 figures were reclassified.

Cash and cash equivalents

Cash and cash equivalents include cash on hand and at banks, funds on call and cash deposits.

Current assets - Financial assets

Investments in debt and equity securities with readily determinable fair values are reported at fair value based upon the last quoted market price, or published net asset value for certain investment funds with characteristics similar to a mutual fund. Publicly traded investments are valued at the last reported sales price on the date of valuation, as quoted on major securities exchanges. Securities that are not traded on major securities exchanges are valued based on quotations received from leading vendors. Forward foreign currency contracts are valued at the average of closing bid and ask quotations from banks and brokers. Pooled investments are funds that are not held at the Fund's custodian bank. These funds are part of multiple investors' commingled funds, which are invested in one or more asset classes by a fund manager. These investments are valued at their closing net asset value per share on the valuation date, which is their redeemable value.

The Fund invests in limited partnerships formed for the purpose of earning returns from alternative investment strategies. Investments in limited partnerships held by the Fund are reported at net asset value as a practical expedient for fair value, which generally represents the Fund's proportionate share of the net assets of the investee partnerships as reported by partnership and reviewed by management for reasonableness. The underlying partnerships in which the Fund invests may hold nonmarketable securities, the fair value of which has been determined by the general partners of the respective partnerships. The Fund's proportionate share of net asset values may differ significantly from the fair values that would have been used had a ready market existed. The Fund's proportionate share of the change in values of the investee partnerships is recorded as a gain or loss on financial assets & investments in the Consolidated Statement of Income and Expenditure. Investments in mutual funds are valued at their closing published net asset value per share on the valuation date, which was their redeemable value.

Securities transactions are recorded on the trade date. Realized gains and losses on security transactions are calculated on the average cost basis.

The Fund invests in various investment securities. Investment securities are subject to various risks such as interest rate, market and credit risks. Due to the level of risk associated with certain investment securities, it is at least reasonably possible that changes in the values of investment securities will occur in the near term and could materially affect the amounts reported in the Balance Sheet.

Non-current assets – Financial assets and Investments

Financial assets, which are traded on a stock exchange, are valued at the stock market closing price prevailing at the end of the year. Investments in companies where the holding is greater than 20% of the share capital are valued using the equity method, unless they are of insignificant value or hold negative equity.

All other financial assets and investments are accounted for at acquisition cost and adjusted for impairment losses, if applicable.

External funding

External funding received from any outside source, whether of a cash or a non-cash nature, is recorded in the books of the Institute upon receipt as Deferred income. External funding received is converted to income when the corresponding expenditure is incurred. Any unspent external funding is deferred to future accounting periods until the corresponding expenditure is incurred or excess

funding is returned to the external funding partner once the project has been concluded. External funding pledged but not received in respect of an expenditure that has been incurred is recorded as income and is accounted for on the balance sheet as External funding receivables.

Tangible and intangible assets
The Institute's expenditure on research equipment & other assets and leasehold improvements is expensed in the year it is incurred in accordance with accepted practice for cancer research organizations. The resale value of research equipment is minimal and no significant income is generated therefrom. With respect to UTI, purchases of equipment and leasehold improvements are capitalized and depreciated.

All operating expenditure, including the cost of patenting and licensing intellectual property, is expensed in the year it is incurred.

Taxes
The Institute and the Fund are tax-exempt organizations and accordingly are not subject to income and capital taxes. UTI is subject to income and capital taxes. Deferred tax assets and liabilities are recognized for future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

Withholding taxes on foreign dividends and interest have been provided for in accordance with the applicable countries' tax rates.

3. Pledged assets
The Institute has pledged assets held by a financial institution to that institution amounting to USD 1.1 million in 2018 and USD 8.4 million in 2017. These amounts are included under Cash & cash equivalents and are used as collateral for various letters of credit amounting to a total of USD 1.0 million. The letters of credit have been issued to the lessors of various office premises occupied by the Institute.

In 2018, the Fund terminated its revolving USD 25.0 million line of credit with a financial institution. At December 31, 2017, there were no amounts outstanding under this agreement. The line of credit was collateralized by qualifying assets with a fair value of approximately USD 85.0 million as at December 31, 2017. The Fund expects to obtain a new line of credit in 2019.

4. Current assets - Financial assets

Financial assets held as current assets as at December 31, 2018 and 2017 were as follows:

	USD	
Description	2018	2017
Financial assets at fair value		
Invested cash and cash equivalents		
- US Dollars	10,327,672	17,134,288
- Other currencies	2,117,217	947,120
Equity investments	64,230,196	92,872,173
Fixed income investments		
- Government	28,409,937	30,696,123
- Corporate	5,586,462	10,404,409
Investments at published net asset value	141,827,906	187,525,530
Due from brokers	17,210,295	55,083,120
Net unrealized (loss) on forward contracts	(62,798)	(369,764)
Financial assets at fair value	**269,646,887**	**394,292,999**
Financial assets at net asset value		
Pooled equity investments	336,810,251	406,772,313
Pooled corporate fixed income investments	91,228,597	84,585,456
Alternative investments (primarily limited partnerships)	697,087,221	596,967,433
Financial assets at net asset value	**1,125,126,069**	**1,088,325,202**
Total financial assets	**1,394,772,956**	**1,482,618,201**

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction among market participants on the measurement date.

Net asset value is the value of an entity's assets minus the value of its liabilities, often in relation to open-end or mutual funds, since shares of such funds registered with the U.S. Securities and Exchange Commission are redeemed at their net asset value.

5. Other short-term receivables

Other short-term receivables of USD 4,842,810 as at December 31, 2018 and USD 5,570,247 as at December 31, 2017 included doubtful debts, which have been fully provided for, in the amount of USD 538,577 in 2017 . In 2018, there is no doubtful debt.

6. Non-current assets - Financial assets

Description	USD 2018	2017
CT Atlantic AG		
Net investment	9,924	10,119
iOx Therapeutics Ltd		
Net investment	33	34
iTeos Therapeutics SA		
Net investment	1,501,274	0
Life Sciences Pharmaceuticals, Inc.		
Net investment	1,457	1,457
Opthea Limited (formerly Circadian Technologies Ltd.)		
Net investment	1,279,365	1,704,224
Premier Veterinary Group plc (formerly Ark Therapeutics Group plc)		
Net investment	2,160	2,672
Serametrix Corporation		
Net investment	100	100
Other		
Fixed income securities	4,879,440	5,135,299
Mutual funds	6,027,825	6,145,579
Loans to staff	40,754	47,154
US 457(b) Pension plan (see Note 14)	1,156,938	1,027,628
Total financial assets	**14,899,270**	**14,074,266**

The Institute is committed to disseminating its know-how to the global research community. The holdings in the start-up organizations shown under Financial assets in the Balance Sheet are the result of licensing arrangements, with start-up organizations or their successors, transferring Institute research knowledge to these companies. Participation in these entities does not form part of the Institute's long term strategy and the respective Financial assets, if not quoted on a stock exchange, are valued at acquisition cost and if applicable, adjusted for impairment losses.

In 2015 iOx Therapeutics Ltd was launched to develop novel cancer immunotherapies discovered through a collaboration between the Institute and the University of Oxford. The company was granted a royalty-bearing license from the Institute, providing rights to intellectual property. The nominal share capital of iOx Therapeutics Ltd, Oxford, United Kingdom is GBP 253.

Until 2017, the investment in iTeos was accounted for using the equity method. iTeos was founded in 2012 and is a joint spin-off of the Institute and the de Duve Institute at the Catholic University of Louvain. Capital of EUR 3.1 million (USD 4.1 million) was raised from the Institute, Hunza Ventures SCA, Life Sciences Research Partners, VIVES Louvain Technology Fund and several angel investors. This financing complements a EUR 6 million non-dilutive grant from the Belgian Walloon Government, which was received in December 2011. iTeos' research program focuses on the development of small molecule immunomodulators that can increase the efficacy of cancer immunotherapy, as well as leverage the spontaneous tumour immune response. Due to a new financing round of USD 75 million in which the Institute did not participate, the Institute's ownership interest of the shares dropped from 37.22% to 6.27%. Due to this dilution of ownership the investment has been reclassified from Investments in 2018 (see also note 7).

The Institute has granted various housing loans to San Diego Branch staff. The outstanding long term receivables amounted to USD 40,754 as at December 31, 2018 and USD 47,154 as at December 31, 2017. Short-term receivables for these loans are recorded under Other short-term receivables and amounted to USD 6,400 in 2018 and USD 9,734 in 2017.

7. Non-current assets - Investments

	USD	
Description	2018	2017
Investment in iTeos Therapeutics SA		
Share capital	0	2,607,780
Share premium	0	2,788,042
Restricted funds	0	1,747,745
Cumulated results	0	12,091,296
percentage owned and voting rights	n/a	37.22%
Net investment at January 1	7,159,217	10,517,124
Share of share premium change	0	4,152
Share of change in restricted funds	0	(454,571)
Share of net loss	0	(3,995,919)
Reduction due to reclassification to non-current Financial Assets	(7,159,217)	0
Translation adjustment	0	1,088,431
Net investment at December 31	**0**	**7,159,217**
Miscellaneous investments	527	527
Total investments at December 31	**527**	**7,159,744**

The investment of iTeos Therapeutics SA has been reclassified to Financial assets (see also Note 6). During 2018, a new financing round of USD 75 million from 3rd party investors was completed and as a result, the Institute's ownership interest of the shares dropped below 20%.

With respect to miscellaneous investments in which the Institute holds at least 20%, the following information is provided:

i. The nominal share capital of Recepta Biopharma S.A., Sao Paulo, Brazil, is BRL 1,000.The company conducts medical research and develops, produces and commercializes humanized antibodies for the diagnosis of human cancer. The Institute holds 26.1% of the shares and of the voting rights.

ii. In order to administer intellectual property assets in areas other than cancer, in 2010 the Institute founded Ludwig Technologies, Inc., Delaware, USA. The nominal share capital is USD 100. Ludwig Technologies, Inc. holds 14.05% of the shares and of the voting rights in the company Extended Delivery Pharmaceuticals, LLC, Connecticut, USA. This biotechnology company is developing a long-acting type of insulin.

iii. In 2010 the Institute entered into a joint venture with The Cancer Research Institute, New York, USA, and formed the company Cancer Vaccine Acceleration Company, LLC, Delaware, USA. The purpose of the company is to identify novel opportunities for the development of cancer vaccine

and immunotherapy and to obtain, hold and develop intellectual property. The nominal share capital is USD 200, of which the Institute holds 50% of the shares and of the voting rights.

8. Tangible fixed assets

During the years ended December 31, 2018 and December 31, 2017 the purchase of equipment and other assets and expenditure on leasehold improvements, amounting to USD 994,884 and USD 1,736,101 respectively, was expensed in the year of acquisition. Receipts arising from the disposal of equipment & other assets amounting to USD 41,376 and USD 4,639 respectively were credited in full to Other operating income.

9. Forward currency contracts

The Fund (in 2018 and 2017) and the Institute (in 2016) entered into forward contracts in order to hedge their exposure to changes in foreign currency rates on their assets and liabilities denoted in foreign currencies. In 2018 and 2017 unrealized gains of USD 114,245 and USD 634,421 and unrealized losses of USD 177,043 and USD 1,291,467 respectively, arose from contracts open at year end. They are included in the Current assets - Financial assets with respect to the Fund, and in Other short-term liabilities with respect to the Institute. They represent the changes in fair value of the contracts from the time of the Fund's and the Institute's conclusion of the contracts.

The notional values of the forward foreign currency contracts held by the Fund and the Institute translated at the relevant year-end exchange rates were as follows:

	USD	
Description	2018	2017
Forward currency purchases	13,661,598	54,755,216
Forward currency sales	13,598,800	54,098,172

10. Pension Schemes

Pension schemes have been established at all Institute locations.

The annual cost of the employers' contributions in 2018 and 2017 for all plans amounted to USD 2,209,972 and USD 2,760,366 respectively and is accounted for as Salaries & social benefits.

The following table shows all the pension schemes for which information is required under Swiss GAAP FER 16. All amounts are in thousands:

USD	Deficit 31.12.18	Share of Commit-ment* 31.12.2018	Share of Commit-ment* 31.12.2017	Net Change in Commit-ment	Contri-butions 2018	Total Income / (Expense) 2018	Total Income / (Expense) 2017
LGI Qualified plan (USA)	(2,337)	(2,337)	(1,567)	(770)	0	(770)	1,027
LGI Supplemental plan (USA)	(7,372)	(7,372)	(7,415)	43	(127)	(84)	(225)
AXA Foundation for Occupational Benefits (CH)	N/A	0	0	0	(410)	(410)	(391)

* Economic commitment

In **Switzerland**, the Institute operates a scheme with the AXA Foundation for Occupational Benefits (AXA) for staff employed in Switzerland. The invested capital amounted to USD 4.9 million as at December 31, 2018 and USD 8.5 million as at December 31, 2017. The capital invested is guaranteed 100% by AXA.

In **Belgium**, a scheme was in place during 2018 and 2017 providing target benefits upon retirement to staff at the Brussels Branch. The plan is administered by and funds are invested with the AG Insurance Company, Brussels. The insurance company recalculates the contributions to be paid to finance the target pension benefits on an annual basis. A new plan was introduced per January 1, 2018, for personnel joining the Institute thereafter. This plan is based on defined contribution and administrated with the AG Insurance company as well.

For the **Stockholm** branch, the Institute operates the Optional ITP Plan 1, a defined contribution scheme, the Optional ITP Plan 2, a defined benefit scheme and the SPP Alternative ITP plan, a defined contribution scheme, with the SPP Life Insurance Company. The plans cover different types of income classes. For the defined benefit schemes the insurance company recalculates the contributions to be paid to finance the target pension benefits on an annual basis.

For the **Uppsala** branch, the Institute operated a defined contribution scheme (Maxplan).

In the **United Kingdom**, the Institute is a registered employer with the Universities Superannuation Scheme (the USS scheme) which, under the defined benefits section, sets the level of contributions based on the advice of the scheme's actuary. The main employer is Universities UK. In view of the size of the scheme and the Institute's limited participation in the management of the scheme, this scheme is treated as a defined contribution scheme. The last triennial actuarial valuation took place on March 31, 2018, and this showed, under the Technical Provisions basis as required by the UK Pensions Regulator, a funding level of 89%. Taking account of the underfunding of the scheme, various changes to the benefit structure are under discussion between the main employer and representatives of the members, the University and College Union. As the Institute has less than 20 active staff members in the scheme, it is not party to the consultation process. It is foreseen that the Institute's financing of the scheme is expected to continue at the employer contribution rate of 18% of the salary.

Following legislation introduced in the United Kingdom in September 2005, special provisions apply in the event of either an employer winding up a pension scheme or causing a cessation event to occur as a registered employer of a multi-employer pension scheme. In these cases, the employer is required to make additional funding available to buyout all liabilities with an insurance company (defined either as "buyout-debt" or "Section 75 debt") or, for multi-employer schemes with continuing indirect participation, to enter into an approved withdrawal agreement (AWA). Subject to agreement with the trustee of the pension scheme and the pension regulator, under an AWA, a guarantee is to be provided by the employer to the trustee of the pension scheme and the additional funding requirement is deferred until the trustee requires it to be paid or the scheme commences wind-up.

The Institute's Board of Directors has reviewed the position taking into account the various on-going employment situations in the United Kingdom. As the USS scheme continues to have active members, and it is intended to retain the scheme for active members, the Board has concluded that there is no need to make provision for buyout-debt as at December 2018 and 2017.

In the event that a buyout-debt liability would be incurred for the USS scheme in the United Kingdom, the cost thereof, based on information provided by the scheme representative using the last triennial valuation of 2017 and current estimation as of end of 2018, is estimated to be GBP 6.9 million (USD 8.7 million) as at December 31, 2018 and GBP 10.3 million (USD 13.9 million) as at December 31, 2017.

In the **United States of America**, the Institute operated The Ludwig Institute for Cancer Research Retirement Savings Plan (the LICRRS Plan). The LICRRS Plan is organized under Section 403(b) of the Internal Revenue Code and is a defined contribution scheme.

The total of short-term liabilities related to pension schemes is set out in Note 11.

In the **United States of America**, The Ludwig Group Inc. (LGI), a wholly owned subsidiary of UTI, maintained both a qualified and a supplemental retirement plan. LGI did not make any contributions to the qualified plan in 2018 or 2017, nor does it expect to make any contributions in 2019. In the supplemental plan, contributions of USD 126,762 were paid in 2018 and USD 126,762 in 2017 . Benefits of USD 1,398,455 in 2017 and USD 1,433,249 in 2017 were paid out in respect of both plans. The qualified plan is funded and the supplemental plan is unfunded. The long-term provisions in respect of the two LGI plans are set out in Note 15.

11. Other short-term liabilities

	USD	
Description	2018	2017
Other short-term liabilities to third parties	1,450,888	1,141,075
Other short-term liabilities to pension funds	19,067	86,963
Other short-term liabilities to governing bodies	7,664	251,100
Total other short-term liabilities	**1,477,619**	**1,479,138**

Other short-term liabilities to third parties include negative replacement values of various forward currency contracts held by the Institute of USD 0 in 2018 and USD 287,280 in 2017.

12. Short-term provisions

USD	Tax related	Other	Total
Provisions as per December 31, 2016	3,397,032	411,949	3,808,981
Additions	0	0	0
Utilizations	0	(317,476)	(317,476)
Release of provisions	(398,838)	0	(398,838)
Currency adjustments	142,553	(1,652)	140,901
Provisions as per December 31, 2017	**3,140,747**	**92,821**	**3,233,568**
Additions	0	0	0
Utilizations	0	0	0
Release of provisions	0	(79,580)	(79,580)
Currency adjustments	(18,953)	(13,241)	(32,194)
Provisions as per December 31, 2018	**3,121,794**	**0**	**3,121,794**

Tax related
The Institute is registered for Value Added Tax (VAT) in Switzerland.

All open VAT reclaims due to the Institute for the years 2000 to 2006, and for the period January 1, 2010 to September 30, 2017, were settled in full by the Swiss Federal Tax Administration in February 2018.

During 2017, the Institute was invoiced for an amount of CHF 3,762,506 (USD 3,807,048) by the Swiss Federal Tax Administration with respect to the amounts claimed by the tax authorities for the years 2007 to 2009.

Of this amount, CHF 2,769,717 (USD 2,802,506) was in respect of VAT claimed by the Swiss Federal Tax Administration for the years 2007 to 2009 and CHF 992,789 (USD 1,004,542) was in respect of interest charged on the tax claimed. The Institute settled the amounts invoiced under reservation, noting that the Institute continues to dispute the claims. The total payment is recorded in the books under Other short term receivables.

Following a reassessment by Institute Management in 2017 of the claims made by the Swiss Federal Tax Administration, it was decided to release the provision in the amount of CHF 398,000 (USD 398,838) from the Tax related provision brought forward from 2016 and credit this amount to Extraordinary income / (expense) (see also Note 17). A total provision of CHF 3,104,000 (USD 3,121,794) continues to be retained with respect to the claims made regarding the years 2007 to 2009.

Other
Various claims have been made by former staff against the Institute in the past. Some of the claims have resulted in court filings. Institute management disputed the claims made and continued to contest them vigorously. During 2018, the last case closed without payment.

13. Deferred income

	USD	
Description	2018	2017
Deferred income at January 1	16,778,023	17,717,142
Usage of deferred income	(9,211,857)	(8,175,617)
Additional deferred income	7,016,675	7,147,764
Exchange rate adjustments	0	88,734
Deferred income at December 31	**14,582,841**	**16,778,023**
Net change in restricted funds	**(2,195,182)**	**(939,119)**

In accordance with the provisions of Swiss GAAP FER 21 all changes in deferred income (restricted funds) are shown gross in the captions External funding and Net change in restricted funds in the Consolidated Statement of Income and Expenditure (see Note 2, Accounting policies and valuation standards - External funding).

14. Other long-term liabilities

Description	USD 2018	2017
US 457(b) Pension plan	1,156,938	1,027,628
Other long-term liabilities - third parties	351,079	401,598
Total other long-term liabilities	**1,508,017**	**1,429,226**

The US 457(b) Pension plan, a non-qualified, tax advantaged deferred compensation retirement plan, is available to some Institute employees in the United States. The Institute provides the plan and the employees defer compensation into it on a pre-tax basis. The total liability includes the return on investment credited to the employee accounts and is offset by a respective financial asset (see Note 6 Non-current assets – Financial assets).

15. Long-term provisions

Long-term provisions relate to the two Ludwig Group, Inc. (LGI) pension plans as described in Note 10.

USD	Total	Supplemental plan	Qualified plan
Provisions as at December 31, 2016	9,911,299	7,317,326	2,593,973
Additions	503,635	224,054	279,581
Utilizations	(1,433,249)	(126,762)	(1,306,487)
Provisions as at December 31, 2017	**8,981,685**	**7,414,618**	**1,567,067**
Additions	2,125,526	84,187	2,041,339
Utilizations	(1,398,455)	(126,762)	(1,271,693)
Provisions as at December 31, 2018	**9,708,756**	**7,372,043**	**2,336,713**

16. Directors' emoluments

Emoluments consist of (i) Directors' fees, (ii) Salaries and social benefits, and (iii) Other remuneration. Directors' fees were paid by the Institute and the Fund; Salaries and social benefits were paid by the Institute and LGI and other remuneration was paid by the Institute.

Description	USD 2018	2017
Directors' fees	335,230	341,432
Salaries & social benefits	1,977,662	1,048,914
Other remuneration	11,378	12,118
Total emoluments	**2,324,270**	**1,402,464**

In 2018 and 2017, the President of the Institute and the Fund and the Institute's Scientific Director received salaries and social benefits but did not receive directors' fees. The Chairperson and the remaining members of the two Boards received directors' fees but did not receive salaries nor social benefits. One member of the Board of Directors received other remuneration in 2018 and 2017.

The remuneration of the two Boards of Directors, the Chairperson of the two Boards, the President of the Institute and the Fund and the Institute's Scientific Director are subject to review by the Institute's and the Fund's Compensation Committees, respectively.

Salaries are benchmarked against objective, third party comparable levels of compensation for fairness and reasonableness. The individual levels of Directors' fees have remained unchanged since 1998.

As at December 31, 2018 the Boards of the Institute and the Fund each had eight members plus an emeritus board member; at December 31, 2017, each had nine members.

17. Extraordinary income / (expense)

For 2018 there are no extraordinary items to report.

The items making up the Extraordinary income for 2017 of USD 667,645 were as follows:
a) Net release of VAT provision of USD 398,838 as referred to in Note 12.
b) Release of provision following repayment of receivable and partial repayment of loan by TC Metrix Sàrl amounting to USD 268,807.

18. Taxes

As a foreign entity, UTI is not subject to U.S. income taxes. The income tax provision relates to taxes for LGI, which conducts its operations in the United States. LGI's pre-tax income was approximately USD 506,000 in 2018 and USD 134,000 in 2017.

On December 22, 2017 the U.S enacted the Tax Cuts and Jobs Act (Tax Reform) into law, which reduced the federal income tax statutory rate from 34% to 21% effective January 1, 2018. The effect of such change in rate reduced the Company's deferred tax assets and increased deferred tax expense by USD 1,237,016 to USD 2,877,301 for the year ended December 31, 2017. For the year ended December 31, 2017, the effective rate of LGI's income tax provision differed from U.S. federal statutory rates of 34% primarily due to the effects of Tax Reform on deferred taxes and state and local income taxes. For the year ended December 31, 2018, the effective rate of LGI's income tax provision differed from the U.S. federal statutory rate of 21% primarily due to the effects of state and local income taxes.

As of December 22, 2018, the Company has completed its accounting with respect to US Tax Reform and has made no adjustments to impact items recorded during the year ended December 31, 2017. The Company also incorporated the new Tax Reform provisions effective for the year ended December 31, 2018. The Company has determined that the Global Intangible Low-taxed Income (GILTI) provision and Base Erosion and Anti-abuse Tax (BEAT) provision are not applicable to the Company. The other new provisions including limitations on interest expense deductibility, limitations on meals and entertainment deductions, and bonus depreciation had immaterial impacts to the Company's income tax provision.

19. Other related party transactions

The Institute is a party to a Research Collaboration and License Agreement with iTeos. Since iTeos was a related party in the fiscal year 2017, income from license fees, external funding and cost recovery amounted to USD 126,136 for the year 2017. As of December 31, 2018, iTeos was not a related party anymore.

20. Collaborative research and lease commitments

All such commitments not recorded in the Balance Sheet, with a notice period of three months or more, are set out by year below:

	USD	
Description	2018	2017
2018	0	25,269,941
2019	31,025,953	25,907,008
2020	30,833,735	25,404,211
2021	29,565,604	25,349,221
2022	29,603,953	26,501,443
2023	4,322,881	2,373,016
2024-2029	375,633	5,204,124
Commitments not recorded in the Balance Sheet	**125,727,759**	**136,008,964**

21. Internal control system and annual risk assessment

The Institute's and the Fund's management are responsible for the design, operation and maintenance of the system of internal control (ICS). The Institute's and the Fund's Boards of Directors are ultimately responsible for the identification and assessment of risks, definition of the ICS framework and monitoring of management actions to ensure the adequacy and effectiveness of the control environment. The Institute's and the Fund's system of internal control over financial reporting is based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) and is designed to provide reasonable assurance regarding the preparation and fair presentation of published financial statements in accordance with generally accepted accounting principles in Switzerland / Financial Reporting Standards – Swiss GAAP FER.

The Institute and the Fund have adopted a risk-based approach to internal control and accept that it is neither possible nor cost effective to build a control environment that is risk free. Accordingly, the system of internal control in place is designed to manage rather than to eliminate risk. The system of internal control is an on-going process designed to identify the principal financial reporting risks, to evaluate the nature and extent of those risks and to manage them efficiently.

In 2018, the Institute's and the Fund's managements conducted risk assessments of the key processes already documented in the form of process flowcharts. Risks within those key processes were identified and evaluated as to their likelihood and impact based on predefined scales, incorporating quantitative and qualitative criteria. For each of the identified risks, the risk level was calculated as a multiple of the likelihood and impact. Top risks for each process were identified based on their respective risk level and classified further as financial reporting or operational risks. Key controls were defined and implemented to mitigate those top financial reporting risks. Non-financial reporting risks are considered to be outside of the ICS and are addressed through other policies and procedures.

The Institute's and Fund's managements assessed the effectiveness of the ICS over financial reporting during the year under review and reported thereon to the Institute's and Fund's Audit Committees.

The respective Audit Committees have the delegated responsibility to oversee the development and operation of the internal control system, to receive reports from the Risk and Compliance Officer

and External Auditors, to review the internal control system documentation and to agree to any actions necessary to implement recommended improvements. The Audit Committees received reports from the Institute's Risk and Compliance Officer with regard to the ICS at all of their respective meetings during the year.

The Boards of Directors of the Institute and the Fund assessed the effectiveness of the ICS for financial reporting throughout the year and believe that the ICS for financial reporting was properly in effect as of December 31, 2018.

As part of the system of internal control, the internal audit function continued to operate and verify the adequacy and effectiveness of internal controls, carry out work to test the controls and provide reports to the two Audit Committees. The operations of the New York Office and the Fund were reviewed by internal audit during 2018 and reports were submitted to the Institute's Audit Committee.

Risk assessments are carried out on an annual basis by the Risk and Compliance Officer reporting to the Audit Committees. They are based on annual self-reassessment of risks and controls by the ICS process owners, information obtained through interviews of the Institute's and the Fund's management and key personnel and further evaluation and testing of controls when carrying out internal audits.

22. Approval of the consolidated financial statements

The consolidated financial statements of the Ludwig Institute for Cancer Research Ltd as at December 31, 2018, together with the Report of the Auditors, dated May 24, 2019, are hereby submitted to the General Meeting of Shareholders.

23. Subsequent events

There are no subsequent events to report, which might have a material impact on the consolidated financial statements.

PERFORMANCE REPORT

Purposes of the organization

The Ludwig Institute for Cancer Research Ltd (the Institute) is an international not-for-profit organization with a more than 45-year legacy of pioneering discoveries relating to cancer. The Institute provides its scientists from around the world with the resources and the flexibility to realize the life-changing potential of their work and advance their discoveries for the benefit of human health. This philosophy, combined with robust translational programs, maximises the potential of breakthrough discoveries.

The Institute conducts its own basic cancer research as well as clinical trials, making it a bridge from the most basic questions of life to the most pressing needs of cancer care. Since its inception, the Institute has invested USD 2.0 billion of its own resources and USD 0.6 billion from external funding in cancer research. Internal support for its research comes from an investment pool valued at around USD 1.4 billion. This investment portfolio is held and managed by LICR Fund, Inc. (the Fund).

The Institute now has around 580 Full Time Equivalent scientists, clinicians, postdoctoral fellows, students and support staff located in five countries who are focused on multiple aspects of cancer research. The Institute is part of the larger Ludwig Cancer Research (Ludwig) community, which also includes the Ludwig Centres at six U.S. institutions, all pursuing breakthroughs to alter the course of cancer.

The Institute's research activities are principally organized through Branches. Each Branch occupies defined space and functions in close association with a local university, research institute and / or not-for-profit hospital. A number of individual investigators, laboratories and centres complement the Institute's Branches through a wide range of collaborative research programs, thereby extending the international reach and research footprint of the Institute.

The Institute continued to attract significant external funding to support its core research programs.

In 2018, the Institute recorded income of USD 12.9 million from industrial and philanthropic resources and USD 8.1 million from Government sources. The total income of USD 21.0 million was 34.0% lower than the 2017 amount received of USD 31.7 million. The decrease in external funding received is mainly related to lower funding for the clinical trials program, funding from the National Institutes of Health and the wind down of the branch in Stockholm.

The five highest providers of external funding to the Institute were as follows: -

US National Institutes of Health – USD 7.7 million, Conrad N. Hilton Foundation, Los Angeles, USA – USD 2.0 million, the Cancer Research Institute, New York, USA – USD 2.0 million, the University of California, San Diego, USA – USD 1.4 million and Université Catholique de Louvain, Brussels, – USD 1.3 million.

The Institute and the Fund prepare, by entity, various statistical and information returns which require analysis of expenditure between i) program service, ii) management and general and iii) grant writing costs.

Using this analysis, on a consolidated basis, for the year 2017 (the latest year where analysis data is currently available), total expenditure of USD 103.7 million is analysed as program service expenditure - USD 79.2 million (76%); management and general expenditure - USD 22.7 million (22%) and grant writing expenditure – USD 1.8 million (2%).

For 2016, total expenditure of USD 105.4 million is analyzed as program service expenditure - USD 83.1 million (79%); management and general expenditure - USD 20.5 million (19%) and grant writing expenditure - USD 1.8 million (2%).

The total operating expenses of USD 91.9 million in 2018 and USD 103.0 million in 2017 consist of the following segments:

	million USD			
Description	2018	2017	Variance	% of total 2018
Branch expenditure				
San Diego (including SMD*)	29.2	30.9	-1.7	32%
Lausanne	7.6	5.2	2.4	8%
Oxford	5.8	8.8	-3.0	6%
Brussels	4.8	8.2	-3.4	5%
Uppsala	2.2	1.7	0.5	2%
Stockholm	0.9	4.7	-3.9	1%
Sao Paulo	0.1	0.2	-0.1	0%
Total Branch Expenditure	**50.6**	**59.7**	**-9.1**	**55%**
Non-Branch expenditure				
Clinical Trials	12.2	14.2	-2.0	13%
Programs	7.9	8.8	-0.9	9%
Intellectual property	2.1	2.2	-0.1	2%
Fund management	7.5	8.3	-0.8	8%
Administration	11.7	9.8	1.9	13%
Total Non-Branch Expenditure	**41.3**	**43.3**	**-2.0**	**45%**
Total Institute	**91.9**	**103.0**	**-11.1**	**100%**

Managing bodies and senior staff

The Statutes and By-laws of the Institute determine the responsibilities and the authority of the following organs of the company: -

the Board of Directors,
Management, comprising the Executive Officers and
Branch Directors.

The Board is elected at the General Meeting of Shareholders held each year in June for a one-year term of office. The members of the Institute's Board of Directors are automatically members of the Board of Directors of the Fund.

The individuals who served as members of the Board of Directors of both the Institute and the Fund during 2018 were as follows: - John L. Notter (Chairperson); Chi Van Dang, MD, PhD; Nancy Ellen

Davidson, MD (+); Olivier Dunant; John D. Gordan III; Samuel Hellman, MD (++); Judge Barbara S. Jones; Adolf E. Kammerer († October 2018); Edward A. McDermott Jr. and Philip A. Pizzo, MD. (+ appointed June 2018; ++ retired June 2018) Richard D.J. Walker retired as Secretary to the Board in November 2018, Alexander Borissov was appointed Secretary to the Board from December 2018.

The Executive Officers of the Institute constitute its management and consisted of the President; the Scientific Director; the Deputy Scientific Director, the Executive Vice-President for Technology Development and the Chief Financial Officer.

These posts were held as of December 31, 2018, by the following individuals: -

President	Edward A. McDermott Jr.
Scientific Director	Chi Van Dang, MD, PhD
Deputy Scientific Director	Robert L. Strausberg, PhD
Executive Vice-President for Technology Development	Jonathan C.A. Skipper, PhD
Chief Financial Officer	Thomas Bänninger

The Executive Officers were supported by: -

Vice-President for Human Resources	Kimberly McKinley-Thomas
Vice-President for Intellectual Property	Pär Olsson, PhD
Vice-President for Communications	Rachel Reinhardt
Vice-President for Clinical Trials Management and Chief Medical Officer	Ralph Venhaus, MD

The Institute has a Scientific Advisory Committee that provides advice to the Scientific Director on scientific matters as well as the review of scientific staff. As of December 31, 2018, the Scientific Advisory Committee was composed of: - Philip D. Greenberg, MD; Victor Velculescu, MD, PhD; Karen H. Vousden, PhD and W.K. Alfred Yung, MD. Robert L. Strausberg, PhD, was the Secretary.

The Branches are each managed by a Director who is responsible for the scientific program as well as the administration of the Branch.

The leadership of the Institute's Branches as of December 31, 2018 was as follows: -

Brussels	Benoît Van den Eynde, MD, PhD
Lausanne	George Coukos, MD, PhD
Oxford	Xin Lu, PhD
San Diego	Richard D. Kolodner, PhD
Stockholm	Thomas Perlmann, PhD

Some Executive Officers, Branch Directors and other senior staff members hold academic positions within the host institutions with which the Institute is associated.

Results of work on Institute research programs in 2018

Scientific Publications

Laboratory and clinical research to further the prevention, early detection, understanding and control of cancer is conducted at the Institute's Branches and through collaborations with other institutions. In 2018, progress was made in the study of tumor biology, cancer genomics, cancer prevention, the tumor microenvironment and tumor immunology.

The Institute is committed to prompt and active dissemination of its research results. In the year 2018, the publication record by location was as follows:

	Primary Research Articles	Reviews/ Book Chapters/ Commentaries	Total
Brussels	16	4	20
Lausanne	47	26	73
NY Collaborative Laboratory	14	10	24
Oxford	40	7	47
San Diego	50	6	56
Sao Paulo	28	3	31
Total	**195**	**56**	**251**

Clinical Trials

Nine Institute-sponsored clinical trials were on-going in 2018. Institute investigational study agents were provided for an additional 12 active clinical trials sponsored and managed by local entities. These 21 trials, together with 7 previously completed studies, were supported by 14 active Institute regulatory dossiers [eight Investigational New Drug (IND) applications (USA), one Drug Master File (DMF), two Clinical Trial Application (CTA) in Switzerland and in the UK, respectively, and three Clinical Trial Notifications (CTN) in Australia]. Over the year, the Institute made no new regulatory submissions and 90 supplemental submissions to its active regulatory dossiers in three countries.

Clinical Trial Sites

The following sites had active LICR-managed trials in 2018:

Australia

- Austin Hospital, Melbourne, VIC, Australia

Switzerland

- Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland

United Kingdom

- Churchill Hospital, Oxford, United Kingdom
- Coventry University Hospital, Coventry, United Kingdom
- Ninewells Hospital, Dundee, Scotland, United Kingdom
- Nottingham City Hospital, Nottingham, United Kingdom
- Southampton General Hospital, Southampton, United Kingdom

North America

- Arizona Oncology, Phoenix, AZ, USA
- Cleveland Clinic, Cleveland, OH, USA
- Dana-Farber Cancer Institute, Boston, MA, USA
- Emory Hospital, Atlanta, GA, USA
- H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA
- Johns Hopkins University, Baltimore, MD, USA
- Mary Crowley Cancer Research, Dallas, TX, USA
- Massachusetts General Hospital, Boston, MA, USA
- Memorial Sloan-Kettering Cancer Center, New York, NY, USA
- Mount Sinai Hospital, New York, NY, USA
- New York University, New York, NY, USA
- Ohio State University Medical Center, Columbus, OH, USA
- Roswell Park Cancer Institute, Buffalo, NY, USA
- Stanford University, Stanford, CA, USA
- University of California (UCLA), Los Angeles, CA, USA
- University of California (UCSF), San Francisco, CA, USA
- University of Miami, Miami, FL, USA
- University of Toledo, Toledo, OH, USA
- University of Virginia, Charlottesville, VA, USA
- Washington University, Saint Louis, MO, USA
- Women and Infants Hospital, Providence, RI, USA
- Yale University, New Haven, CT, USA

Technology Development

One of the main objectives of the Institute is to translate its scientific discoveries to the benefit of the public as quickly and effectively as possible. In accordance with this objective, the Institute's research activities stretch beyond its initial discoveries, to encompass the determination of how they might be further developed and ultimately benefit cancer patients. Given that the significant costs involved in drug development are far beyond the resources available to it, the Institute enters into research, development and licensing agreements with commercial drug development organizations having the financial, management and technological resources necessary to develop Institute discoveries for diagnostic and therapeutic purposes.

To facilitate this work, the Institute has, in addition to building in-house competence to initiate and manage early phase clinical trials, developed a comprehensive patent protection and licensing program. Several new patents were issued and technology licenses were completed this past year. In 2018, 12 new US patents, two new European patents and one Swiss trademark were issued, and 13 new US applications and a further five new international patent applications were filed. In addition, the Institute was party to 190 license, sublicense and option agreements with commercial organizations at the start of 2018. During the year, an additional seven agreements were implemented while nine agreements either expired or were terminated. At the end of 2018 the Institutes portfolio comprised a total of 188 agreements. The majority of these license agreements allow companies to commercialize Institute reagents or products derived from such technologies for laboratory research purposes, as companion diagnostic candidates or for a company's own in-house commercial research. A subset of these agreements grant rights to commercial entities using Institute discoveries for the development of therapeutic and diagnostic products. These development programs are at various stages of product development, from pre-clinical testing to phase 1, 2 and 3 clinical trials. One marketed product Sargramostim (or Leukine), a recombinant granulocyte macrophage colony-stimulating factor (GM-CSF), is used for myeloid reconstitution after bone marrow transplantation or neutropenia induced by chemotherapy.

The gross income to the Institute from the commercialization of Institute discoveries was USD 3.8 million in 2018. The significant contributions to the gross income were represented by royalty income from the sale of GM-CSF, plus the sales of numerous research reagents and kits. Additional licensing payments were received following certain development milestones being reached in the development of therapeutic antibody programs. The net income to the Institute after sharing with co-owners and inventors was USD 2.1 million.

Immunotherapy of cancer continues to be a focus of the Institute's translational and clinical research, which is reflected in the patents issued and filed by the Institute and its partners. In addition, the discovery and patenting of new genomic methods and related technologies reflects the Institute's established expertise in the field and an emerging focus in seeking useful applications for its genomics applications and know-how.

The Institute has ongoing clinical research collaborations with several pharmaceutical and biotechnology companies including Medimmune/AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, CureVac, Oncovir, and Targovax. Most of these collaborative studies are being conducted in collaboration with the Cancer Research Institute, New York (CRI), and are designed to evaluate cancer immunotherapy PD-1/L1 drug combinations to improve the clinical impact of these therapies for cancer patients. During 2018, the Institute was sponsoring nine active clinical trials, with four

clinical trials open for patient enrollment. Results from some of the Institute's clinical trials were presented at several major international congresses in 2018:

Clinical Study	Event
Phase 1 study of NY-ESO-1 vaccine + ipilimumab in patients with unresectable or metastatic melanoma (NCT01810016)	Annual Meeting of the American Society for Clinical Oncology, June 2018
Phase 1/2 study of mRNA vaccine therapy + durvalumab ± tremelimumab in patients with metastatic non-small cell lung cancer (NCT03164772)	Annual Meeting of the American Society for Clinical Oncology, June 2018
Phase 1 study to evaluate safety and efficacy of ipilimumab + nivolumab + external beam radiotherapy in patients with metastatic melanoma (NCT02659540)	Annual Meeting of the American Society for Clinical Oncology, June 2018
Phase 1 Study to Evaluate the Safety and Tolerability of Durvalumab and Tremelimumab in Patients with Advanced Solid Tumors (NCT01975831)	Fourth CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference, September 2018
Phase 1/2 Study to Evaluate Durvalumab + ONCOS-102 Administered by Intraperitoneal Infusion in Patients with Epithelial Ovarian or Metastatic Colorectal Cancer who have Peritoneal Disease (NCT02963831)	Fourth CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference, September 2018
Phase 1/2 Study of mRNA Vaccine Therapy + Durvalumab ± Tremelimumab in Patients with Metastatic Non-small Cell Lung Cancer (NCT03164772)	Fourth CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference, September 2018
Phase 1/2 Study of chemo-immunotherapy with durvalumab and pegylated liposomal doxorubicin in platinum-resistant recurrent ovarian cancer (NCT02336165)	Annual Meeting of the European Society for Medical Oncology, October 2018
Phase 1 Clinical Trial of Ipilimumab, Nivolumab and Radiation Therapy for Patients With Metastatic Melanoma (NCT02659540)	Annual Meeting of the American Society for Radiation Oncology, October 2018
Phase 2 Study to Evaluate the Clinical Efficacy and Safety of Durvalumab and Bevacizumab in Bevacizumab-naïve Patients with Recurrent GBM: Results for Cohorts B2 and B3 (NCT023366165)	Annual Meeting of the Society for Neuro-Oncology, November 2018

Checkpoint antibody immunotherapies targeting PD-1/L1 and CTLA-4 have resulted in dramatic improvements in disease outcome in certain cancer patients. However, the majority of advanced stage patients do not respond or subsequently relapse following treatment with existing checkpoint immunotherapies, so continued research with additional or complementary immune modulatory agents remains a critical endeavor. The novel checkpoint agonist antibodies INCAGN01876 (anti-GITR), and INCAGN01949 (anti-OX40) originated from the Institute's collaboration with Agenus Inc. These are being developed by the company Incyte and are being evaluated in ongoing phase 1/2 clinical trials as single agents and in combination studies with Nivolumab (anti-PD1) and Ipilimumab (anti-CTLA-4). In 2018, patient recruitment was completed in two clinical trials of INCAGN01949 and one clinical trial of INCAGN01876.

Separately, Agenus is developing additional antagonist checkpoint antibodies AGEN2034 (anti-PD1) and AGEN1884 (anti-CTLA-4) originating from the Institute collaboration. By mid-2018, more than 100 patients with advanced refractory cancer had received AGEN2034 and/or AGEN1884 in single agent clinical trials. Both antibodies were well tolerated and the recommended phase 2 dose for each antibody was selected for a subsequent phase 2 trial of the AGEN2034 and AGEN1884 combination in cervical cancer, launched in 2018. Agenus also initiated a phase 2 clinical trial of AGEN1884 (anti-CTLA-4) in combination with Pembrolizumab (anti-PD1) in first line non-small cell lung cancer during 2018. In addition, Agenus also revealed that it is developing a next generation anti-CTLA-4 antibody (AGEN1181), which is a modified version of AGEN1884 with improved biological activity and potential clinical benefit.

Ludwig start-up company iTeos Therapeutics Ltd (iTeos) is dedicated to the development of immuno-oncology therapies targeting the tumor microenvironment. In 2018 iTeos completed a $75M series B capital round led by MPM Capital with additional new investors HBM Partners, 6 Dimensions Capital and Curative Ventures. In connection with this capital increase, a US subsidiary (iTeos Inc) was established in Cambridge, MA, to support the clinical development of its lead cancer immunotherapy programs: EOS100850, an adenosine A2A receptor antagonist; and ESO884448, a fully human anti-TIGIT antibody.

TGFβ is increasingly recognized as a potential key mechanism of immune system evasion by tumor cells. Specifically, TGFβ may modify the local tumor microenvironment, attenuating tumor response to established checkpoint blockade therapies (anti-PD/L1). To better understand the contribution of the individual TGFβ ligands to this anti-tumor activity, isoform-specific anti-TGFβ monoclonal antibodies have been developed by the Institute. In preclinical studies these were shown to be effective in delaying in vivo tumor growth in melanoma and breast cancer models (AACR 2018). In addition, the humanized anti-TGFβ monoclonal antibodies retain mono-isoform selectivity for TGFβ1 or TGFβ3 and the ability to neutralize TGFβ-driven signaling (SITC 2018). An alternative approach to targeting TGFβ derived tumor immunosuppression involves targeting the GARP/latent TGFβ complex. Ludwig investigators together with collaborators at the de Duve/UCL in Brussels and biotechnology company Argenx, previously generated monoclonal antibody ARGX-115 (anti-GARP). Argenx completed preclinical IND studies with ARGX-115 in 2018, resulting in the pharmaceutical company Abbvie Inc exercising an option agreement, granting it an exclusive license to develop and commercialize the anti-GARP antibody.

Ludwig's genomic technologies have generated significant commercial interest. Ludwig start-up Arima Genomics is developing sequencing technologies licensed from Ludwig into kits utilizing a modified version of the standard Hi-C protocol to capture 3-dimensional chromosome

conformational information. In 2018, Arima completed a successful early-access program and subsequent commercial launch of its Arima-HiC genomic sequencing technology.

At the end of 2018, the Institute had holdings in ten start-up companies with products at various stages of development and maturity originating from licenses to Institute technology:

- CT Atlantic AG (in liquidation), Switzerland
- Cancer Vaccine Acceleration Company, LLC, USA
- Extended Delivery Pharmaceuticals, LLC, USA
- iOx Therapeutics Ltd, United Kingdom
- iTeos Therapeutics SA, Belgium
- Life Sciences Pharmaceuticals, Inc, USA
- Opthea Limited, formerly Circadian Technologies Limited, Australia
- Premier Veterinary Group plc, formerly Ark Therapeutics Group plc, United Kingdom
- Recepta Biopharma S.A., Brazil
- Serametrix Corporation, USA

Human Resources

An important aspect of the Institute's developing programs is the training of outstanding young scientists who will in time join an emerging new generation of cancer investigators. During the year, 9 PhD students started their postgraduate training with the Institute and 8 completed their training with the Institute. At December 31, 2018, the Institute was sponsoring 51 postdoctoral fellows and 30 PhD students.

Awards and Distinctions

The quality of the Institute's investigators continued to be internationally recognized. The following awards and distinctions were received in 2018:

Brussels

Stefan N Constantinescu, MD, PhD	Professeur ordinaire, Université catholique de Louvain

Lausanne

George Coukos, MD, PhD	Named 2018 scientific personality of the year
Johanna Joyce, PhD	Recipient of 2018 Cloetta Prize
Ping-Chih Ho, PhD	Recipient of the 2018 Swiss Bridge Award
	Awarded the ERC Starting Grant 2018
	Recipient of the 2018 Anna Fuller Prize
Camilla Jandus	Award of the 2018 Swiss National Science Foundation PRIMA (recognition grant for women researchers)
	Awarded the Privat-Docent academic title
	Recipient of the 2018 Dr. Ettore Balli Foundation Prize

NY Collaborative Laboratory

Jedd D. Wolchok, MD, PhD	Recipient of the 2018 Fellow of the American Society of Clinical Oncology (FASCO) distinction
Roberta Zappasodi	Recipient of the IBM-Bio4Dreams Award "Identification of non-conventional inhibitory T cells as a biomarker of immune checkpoint blockade."
	Recipient of the 2018 SITC Sparkathon Award
	Recipient of the 2018 PICI Bridge Scholar Award
Luis Filipe Campesato:	Recipient of the 2018 AAI Trainee Abstract Award

Oxford

Sir Peter J. Ratcliffe, MD, FRS	Recipient of the 2018 Massry Prize

San Diego

Webster K. Cavenee, PhD	Recipient of 2018 Helen Keller Award in Vision Research
	Recipient of the 2018 Weinman Award in Cancer Research
Dhanya Cheerambathur, postdoctoral fellow	Recipient of the 2018 Wellcome-Beit Prize
Don W. Cleveland, PhD	Recipient of the 2018 Breakthrough Prize in Life Sciences or Mathematics
	Recipient of the NOMIS Distinguished Scientist Award 2018